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acid itself was then crystallised from 30 c.c. of light petroleum and dried at 100° (specimen B).

(A) froze at 70·86°, corresponding to 42·25% of 9-ketostearic acid, this value being selected instead of the alternative on the other branch of the curve on account of the following observations. A mixture of (A) (0·3222 g.) with 10-ketostearic acid (0·0383 g.) froze at 72·20°, corresponding to 38·25% of 9-ketostearic acid. Hence (A) contains 42·57% of 9-ketostearic acid. A mixture of (A) (0·3222 g.) with 10-ketostearic acid (0·0802 g.) froze at 73·27°, corresponding to 34·0% of 9-ketostearic acid. Hence (A) contains 42·46% of 9-ketostearic acid. The mean value is 42·42% of 9-ketostearic acid. (B) froze at 70·90°, corresponding with 42·10% of 9-ketostearic acid, and a mixture of (B) (0·4730 g.) with 10-ketostearic acid (0·0376 g.) froze at 71·75°, corresponding with 39·60% of 9-ketostearic acid. Hence (B) contains 42·75% of 9-ketostearic acid and the mean value is 42·42% of 9-ketostearic acid. The close approximation of the mean values for (A) and for (B) is no doubt a coincidence, but the products are identical because a mixture of 1 part of (A) (f. p. 70·77°) and about 2 parts of (B) (f. p. 70·90°) had f. p. 70·86°. It is believed that the errors in the estimated percentage compositions of (A) and (B) do not exceed 0·5.

We wish to express our thanks to the Food Investigation Board for grants which enabled one of us to take part in this investigation.

THE UNIVERSITY, MANCHESTER. [*Received, June 1st,* 1926.]

CCXCIII.—*Researches in the Menthone Series. Part II. Optically Active Menthones and Menthylamines.*

By JOHN READ and GEORGE JAMES ROBERTSON.

IN the first communication of this series (J., 1925, **127**, 2782), it was shown that *dl*-piperitone could be used as a source of derivatives of either *dl-iso*menthone or *dl*-menthone, since the *dl-iso*menthone which it yields upon reduction may be readily converted into a mixture of these two ketones. A detailed study of the conditions regulating the interconversion of menthone and *iso*menthone then became essential in developing the research. Attention was therefore directed to the optically active forms of the ketones, in which the changes under consideration could be followed polarimetrically; so that the problem of isolating such forms in a state of purity was in turn brought within the ambit of the investigation.

The purest specimen of *l*-menthone prepared by Beckmann (*Annalen*, 1889, **250**, 335) had $[\alpha]_D$ −28·46°, but that this is not an ultimate value is demonstrated by our preparation in the same way

401359

of a specimen having $[\alpha]_D^{20°}$ −29·60°, whilst Pickard and Littlebury (J., 1912, **101**, 124) also recorded the value $[\alpha]_D^{19°}$ −29·10°. *d*-Menthone having $[\alpha]_D^{18°}$ +24·85° was also prepared by these investigators (*loc. cit.*). The availability of piperitone in *d*- and *l*-forms has rendered possible the ready production, by catalytic hydrogenation, of specimens of *l*- and *d*-*iso*menthone, having the respective maximum values $[\alpha]_D^{15°}$ −71·41° and +69·10°.

These specimens, together with *l*-menthone, were used in investigating further the "inversion" of *l*-menthone, first observed by Beckmann (*Annalen*, 1889, **250**, 334) and attributed by Tutin and Kipping (J., 1904, **85**, 66) and Gardner, Perkin, and Watson (J., 1910, **97**, 1756) to a temporary suppression of the asymmetry of carbon atom (4) through enolisation of the adjacent keto-group. The experiments summarised below show that with energetic reagents, such as melting 90% sulphuric acid or alcoholic sodium ethoxide, definite equilibria are rapidly attained between *l*-menthone and *d*-*iso*menthone, the values of $[\alpha]_D^{15°}$ for the equilibrated material being approximately +26° for the former reagent and +7° for the latter, under the conditions adopted. These equilibria were realised experimentally, starting from *d*-*iso*menthone, as well as from *l*-menthone. With certain other reagents the equilibrium is attained much more slowly, so that the expression "inversion" is sometimes not strictly applicable to either of the ketones. Thus the chromic acid mixture used in preparing *l*-menthone from *l*-menthol brings about a comparatively slight fall in the rotatory powers of *l*-menthone and *d*-*iso*menthone. Of special interest also is the marked difference in the equilibrating action of heat at 180° and 200°, since *l*-piperitone, in which the asymmetry is associated solely with carbon atom (4), exhibits parallel behaviour (J., 1923, **123**, 2269), although it is affected only slightly by treatment with cold 90% sulphuric acid (*loc. cit.*, p. 2271). The action of other reagents commonly used in operations dealing with the menthones was also investigated with the aim of imparting precision to the study now in hand of reactions involving the use of the optically active and externally compensated forms of these substances. Similar observations made with *l*-*iso*menthone confirmed the existence of the equilibrium *d*- (or *l*-)*iso*menthone $\rightleftharpoons$ *l*- (or *d*-)menthone.

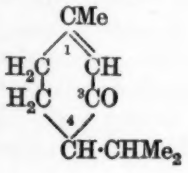
It is at present impracticable to calculate accurately the composition of the various equilibrium mixtures, owing to the uncertainty concerning the maximum optical rotatory powers of *l*- (or *d*-)menthone and *d*- (or *l*-)*iso*menthone. Since *l*-menthone of $[\alpha]_D^{20°}$ −29·60° when carefully oximated at the ordinary temperature in the absence of alkali yielded an apparently homogeneous specimen of *l*-menthoneoxime, it would appear to possess a high degree of

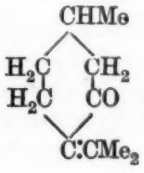
purity. On the other hand, in spite of the high optical rotation, the purity of the preparations of *l*- and *d*-*iso*menthone now described is questionable, since a specimen of the latter having $[\alpha]_D^{20°}$ +65·14° furnished an appreciable quantity of *dl*-*iso*menthone-α-semicarbazone when treated with semicarbazide acetate (J., 1923, **123**, 2924); as the optically active *iso*menthones are incapable of racemising to *dl*-*iso*menthone under such conditions, the presence of *dl*-*iso*menthone in the specimen denotes the presence of *dl*-piperitone in the *l*-piperitone originally used. Whether the implied partial racemisation of the *l*-piperitone was antecedent to the process of hydrogenation is not clear, but the appreciably higher value now noted for *d*-piperitone from the oil of *Andropogon Jwarancusa* suggests the possibility of a slight racemic contamination of the purest *l*-piperitone yet isolated from the oil of *Eucalyptus dives*. A further indication of such contamination may perhaps be discerned in the fact that the oximes prepared from *d*- and *l*-*iso*menthone have as yet been obtained only in the form of viscid oils, the respective values of $[\alpha]_D^{15°}$ being +46·0° and −45·2° in absolute alcohol. A mixture of equal amounts of these two preparations, however, yielded crystalline *dl*-*iso*menthoneoxime, melting at 99—100°, identical with the substance recently described by Read and Cook (J., 1925, **127**, 2785).

Attempts to prepare specimens of *iso*menthone of higher optical rotation by the catalytic hydrogenation of *d*-pulegone (II) and *l*-Δ⁴-*p*-menthen-3-one (III), in the manner originally adopted for *l*- and *d*-piperitone (I), led to the results summarised below:

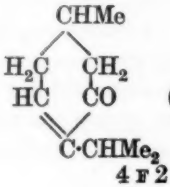
Unsaturated ketone.	$[\alpha]_D^{15°}$ of unsaturated ketone.	$[\alpha]_D^{15°}$ of derived *iso*menthone.
d-Piperitone	+62·50°	−71·41°
l-Piperitone	−53·90	+69·10
d-Pulegone	+23·60	+33·45
l-Δ⁴-*p*-Menthen-3-one	−78·36	+43·24

The products formed in the last two instances were proved to consist of mixtures of *l*-menthone and *d*-*iso*menthone; it should be noticed, however, that these results do not necessarily indicate a similar qualitative composition for the products derived from *d*- and *l*-piperitone, since in these instances the spatial additive process is conditioned not by the asymmetry of carbon atom (1), but by that of carbon atom (4):

(I.) 



(II.)

(III.) 

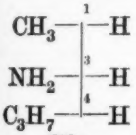
As examples of the confusion hitherto existing in the chemistry of the menthones it may be noted that Skita and Ritter (*Ber.*, 1910, **43**, 3394) identified the product obtained by the catalytic reduction of *d*-pulegone as partly racemised *d*-menthone; moreover, Wallach (*Annalen*, 1913, **397**, 214) characterised the ketone prepared similarly from *l*-Δ^4-*p*-menthen-3-one as *l*-menthone.

As a result of the "inversion" experiments discussed above, the possibility was next considered of preparing *d*- and *l-iso*menthone by oxidising the corresponding optically active *iso*menthols with chromic acid mixture. The results of a simultaneous research (following paper) dealing with optically inactive menthylamines and menthols derived ultimately from *dl*-piperitone, indicated a line of approach through the corresponding *iso*menthylamines. This indication appeared also to be in keeping with a brief mention by Beckmann (*Ber.*, 1909, **42**, 846) of a *d-iso*menthone having $[\alpha]_D$ +93·2°, originating from a supposed *d-iso*menthylamine hydrochloride. The last-named substance, prepared from the reduction product of the mixture of oximes yielded by "inverted" *l*-menthone, had $[\alpha]_D$ +17·7°. Wallach, however, had stated that the liquid oxime from "inverted" menthone having $[\alpha]_D$ +15·0° gave mainly *l*-menthylamine when reduced (*Annalen*, 1893, **276**, 313); since, moreover, Wallach had described a so-called "R-menthylamine" hydrochloride having $[\alpha]_D$ +17·2° (*loc. cit.*, pp. 306, 324), it became necessary to submit the whole field comprehended by these observations to a careful experimental enquiry.

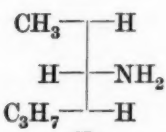
In the first place, it was found possible to prepare Wallach's "R-menthylamine" by heating either *l*-menthone, *d-iso*menthone, or mixtures of these ketones with dry ammonium formate, in accordance with the original method. For the reasons outlined below, this base is considered to be derived from *l*-menthone: following the accepted nomenclature (compare Pickard and Littlebury, J., 1912, **101**, 109), it should thus be termed *d-neo*menthylamine. The value $[\alpha]_D^{15°}$ +21·5° was observed for the hydrochloride of the pure base in dilute aqueous solution, but on the whole the data now recorded are in satisfactory agreement with the observations of Wallach. The base is distinguished by the solubility of its hydrochloride in light petroleum, and in general by the beauty of its crystalline derivatives. Pure formyl-*l-neo*menthylamine has also been prepared from *l-iso*menthone. When treated with nitrous acid, *d-neo*menthylamine yields a product consisting mainly of partly racemised *d*-Δ^3-menthene, so that, unlike *l*-menthylamine, it cannot be utilised as a source of the related menthol and menthone.

The crude menthylamine hydrochloride, having $[\alpha]_D^{15°}$ −12·5°, obtained by reducing the viscid product formed in oximating

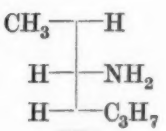
"inverted" *l*-menthone, proved to consist of a mixture of which the components could not readily be separated by fractional crystallisation. From the viscid oxime of *d-iso*menthone, however, was obtained similarly a crude menthylamine hydrochloride having $[\alpha]_D^{15°}$ +20·63°, and a single recrystallisation furnished a homogeneous hydrochloride with $[\alpha]_D^{15°}$ +23·60°. In spite of the approximately identical rotatory power, this substance differs markedly from *d-neo*menthylamine hydrochloride by reason of its high melting point and its insolubility in light petroleum or in ether. Moreover, other corresponding derivatives of the two bases exhibit wide differences in rotatory power as well as in melting point and solubility. In view of its preparation from *iso*menthone, this base is to be regarded as an *iso*menthylamine. Upon treatment with nitrous acid, it yields a crystalline dextrorotatory *iso*menthol; the name *d-iso*menthylamine thus appears to be appropriate, since the prefix *neo-* as applied above is associated with the conversion of the base in this way to a menthene and not to a menthol. According to Wallach (*Annalen*, 1898, **300**, 278), the conversion of a menthylamine to a menthene by nitrous acid is conditioned by the *cis*-disposition of -NH_2 and -H, attached respectively to carbon atoms (3) and (4); adopting further the *trans*-configuration for *iso*menthone (compare Meyer u. Jacobson, "Lehrbuch der organischen Chemie," 1923, II, i, 894), *iso*menthylamine may be represented by configuration (VI) and menthylamine by configuration (IV), since both these bases yield a menthol on reaction with nitrous acid:



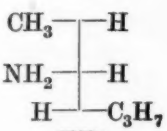
(IV.)
l(or *d*)-Menthylamine.



(V.)
d(or *l*)-*neo*-Menthylamine.



(VI.)
d(or *l*)-*iso*-Menthylamine.

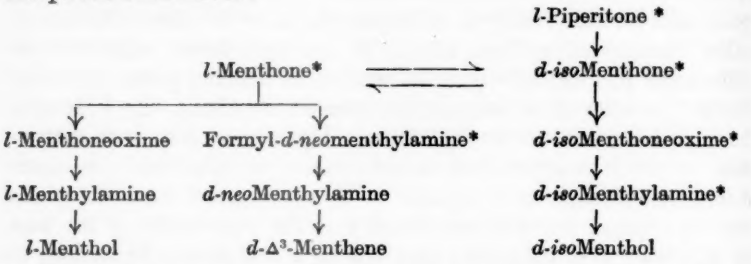


(VII.)
neoiso-Menthylamines.

According to the experimental evidence, the base designated above as *neo*menthylamine might be either (V) or (VII). The adoption of configuration (VII), however, would imply that the reversal of the asymmetry of carbon atom (3) of configuration (VI) has practically no influence on the optical rotation, the respective values for the hydrochlorides being +23·60° and +21·50°. Such a result appears extremely less likely than the corresponding change from −36·60° (*l*-menthylamine hydrochloride) to +21·50° (*d-neo*menthylamine hydrochloride) indicated by the scheme as given.

Certain optically pure derivatives of *l-iso*menthylamine have also been prepared from the viscid oxime of *l-iso*menthone, and the

preparation and characterisation of *dl-neo*menthylamine and *dl-iso*menthylamine, together with a derived *dl-iso*menthol, are described in the next communication. The only menthylamines remaining to be prepared are thus the *neoiso*menthylamines corresponding to configuration (VII). The operations dealt with in this contribution may be summarised as follows, the changes distinguished by an asterisk having been accomplished also with the enantiomorphous substances :



It is hoped that the somewhat tedious process, now in hand, of accumulating sufficient *d* (and *l*)-*iso*menthol for complete characterisation and oxidation to *d* (and *l*)-*iso*menthone may at last render practicable the realisation of an ideal expressed some years ago, which has influenced the course of this series of investigations, originating in turn from a study of the chemistry of piperitone: " Es wäre eine dankbare Aufgabe, die vier optisch aktiven und die beiden wahren racemischen Modificationen von krystallisirbaren Menthon-Derivaten darzustellen und unter besonderer Berücksichtigung der modernen, von van 't Hoff und Roozeboom vertretenen Anschauungen genau zu untersuchen, da dieser Fall von grundlegender Bedeutung für die Terpenchemie ist " (Meyer u. Jacobson, *op. cit.*).

Experimental.

Conditions affecting the Dynamic Equilibrium between l-*Menthone and* d-iso*Menthone.*

1. The following results were yielded by specimens of *l*-menthone having $[\alpha]_D^{20°}$ −29·60° and prepared by oxidising *l*-menthol. When treated with melting 90% sulphuric acid (*Annalen*, 1889, **250**, 334), the resulting ketone exhibited values of $[\alpha]_D^{20°}$ ranging from +11·0° to +25·7°; it would appear that the more quickly the menthone is extracted from the aqueous acid after pouring over ice, the higher is the specific rotation in the dextro sense. When dissolved in 98% formic acid and maintained at 40° for 4 hours, the recovered ketone had $[\alpha]_D^{20°}$ +13·0°. Upon passing dry hydrogen chloride into ice-cooled *l*-menthone and keeping the deep yellow

solution for a day, the recovered ketone had $[\alpha]_D^{20°}$ +5·2°. Upon adding *l*-menthone to concentrated hydrochloric acid cooled in ice, and then warming the mixture to 30°, the value of $[\alpha]_D^{20°}$ changed to +3·7°. After the ketone had been boiled under reflux for 30 minutes with a 20% solution of oxalic acid, the specific rotation had changed to −21·8°. *l*-Menthone was affected only slightly by the chromic acid mixture used in its preparation from *l*-menthol (*loc. cit.*, p. 325), the specific rotation after a second contact with this reagent being −27·0°. When *l*-menthone was shaken at intervals for a day with 25% aqueous potassium hydroxide the specific rotation changed to −23·6°. Upon adding *l*-menthone (10 g.) to absolute alcohol (40 c.c.) in which sodium (1·5 g.) had been dissolved and keeping the mixture for 20 hours, the recovered ketone had $[\alpha]_D^{20°}$ +6·8°; this specimen, when treated with melting 90% sulphuric acid, reverted to the value $[\alpha]_D^{20°}$ +24·8°. In the above operations, the ketone was recovered from the reaction mixture by dilution with water, or pouring on to ice, followed by extraction with ether or chloroform. When *l*-menthone was kept at 180° in a glass vessel, the specific rotation changed to −10·6° in 3 hours and to −8·2° in 7·5 hours; upon then raising the temperature to 200°, the values of $[\alpha]_D^{20°}$ after 4 and 14 hours were +6·2° and +14·8°, respectively, the last value remaining unaltered after a further period of 16 hours at 200°. Repeated distillation in steam or under diminished pressure had no appreciable effect on the specific rotation of *l*-menthone.

2. Specimens of *d-iso*menthone, prepared by hydrogenating *l*-piperitone and having values of $[\alpha]_D^{20°}$ ranging from about +57° to +65°, gave equilibrium values corresponding closely to those recorded above when submitted to similar processes. Upon treating a specimen having $[\alpha]_D^{20°}$ +59·26° successively with melting 90% sulphuric acid, alcoholic sodium ethoxide, and again with sulphuric acid, the corresponding values of $[\alpha]_D^{20°}$ were +26·8°, +7·2°, and +23·4°. When *d-iso*menthone with the maximum value of $[\alpha]_D^{15°}$ +69·10°, prepared in the same way from *l*-piperitone having $[\alpha]_D^{15°}$ −53·90°, was added to chromic acid mixture at 30° and treated in the manner adopted by Beckmann (*loc. cit.*, p. 325) in the preparation of *l*-menthone, the value declined only to $[\alpha]_D^{15°}$ +59·3°.

The Dynamic Equilibrium between d-*Menthone and* l-iso*Menthone.*

The *d*-piperitone used as the starting point in this section of the work was isolated from the essential oil of *Andropogon Jwarancusa* by fractional distillation under diminished pressure (J., 1923, **123**, 2269). The necessary material was kindly collected and distilled

in the autumn of 1923 by Colonel C. R. Johnson, Abbottabad, to whom, as also to Professor J. L. Simonsen, we express our cordial thanks. The crude oil afforded a 68% (vol.) yield of *d*-piperitone, b. p. 95—97°/7·5 mm., $n_D^{16\cdot5°}$ 1·4860, $\alpha_D^{15°}$ +58·42°, $[\alpha]_D^{15°}$ +62·50°. The hydrogenation to *l-iso*menthone was conducted essentially as described by Hughesdon, Smith, and Read (J., 1923, **123**, 2920), but it was found advantageous to initiate the operation at 30° and to accelerate the stirring. The yield of *l-iso*menthone was 76% of the theoretical amount, and the following physical constants were observed for the refractionated material: b. p. 79—80°/7 mm., $n_D^{12°}$ 1·4580, $\alpha_D^{15°}$ −64·24°, $[\alpha]_D^{15°}$ −71·41°.

When treated with melting 90% sulphuric acid, as described above for *l*-menthone, this specimen of *l-iso*menthone gave a product having $[\alpha]_D^{15°}$ −14·3°. Further, a second portion of the same specimen had $[\alpha]_D^{15°}$ −5·7° when recovered from a solution in absolute-alcoholic sodium ethoxide. The corresponding values of $[\alpha]_D^{15°}$ for the *l*-menthone–*d-iso*menthone equilibrium, recorded above, are +11·0° to +25·7° and +6·8°, respectively.

The Catalytic Hydrogenation of d-*Pulegone.*

Upon submitting oil of pennyroyal (400 c.c.) of French origin (stated to be from *Mentha Pulegium*) to three successive fractional distillations under diminished pressure, a specimen of pulegone (170 c.c.) was obtained with the following characteristics: b. p. 96·6—97·6°/12·5 mm., $n_D^{15°}$ 1·4852, $[\alpha]_D^{15°}$ +23·60°. When hydrogenated at 20° in presence of colloidal palladium, in accordance with the method adopted for *l*-piperitone (J., 1923, **123**, 2921), *d*-pulegone (35 g.) absorbed the theoretical quantity of hydrogen in 2·5 hours. The product was extracted with ether and purified by distillation under diminished pressure: the menthone fraction amounted to about 80% of the calculated yield, and the higher fraction had an odour of menthol. The refractionated menthone distilled at 81—82°/11 mm., and had $n_D^{15°}$ 1·4561, $[\alpha]_D^{15°}$ +26·17°, and $d_{4°}^{15°}$ 0·900. In two similar experiments, owing to some unknown adverse condition, hydrogenation was incomplete; the first fractions (b. p. 89—94°/13 mm.) were accordingly mixed and rehydrogenated at a temperature which gradually declined from 30° to 15°. The refractionated menthone distilled at 86—88°/13 mm. and had $n_D^{15°}$ 1·4555 and $[\alpha]_D^{15°}$ +30·80°. The highest value of $[\alpha]_D^{15°}$ observed for a specimen of menthone prepared in this way was +33·45°.

When the specimen of menthone having $[\alpha]_D^{15°}$ +30·80° was treated with melting 90% sulphuric acid, the specific rotation fell to $[\alpha]_D^{15°}$ +27·07°, whilst renewed treatment with alcoholic sodium ethoxide brought about a further decline to $[\alpha]_D^{15°}$ +7·93°. These inversion

experiments show definitely that the product obtained by hydrogenating *d*-pulegone consisted of a mixture of *d-iso*menthone and *l*-menthone; this view is also supported by the fact that the oxime furnished by this product was an oil which could not be induced to crystallise.

The Catalytic Hydrogenation of l-Δ^4-p-*Menthen*-3-*one.*

In order to ensure the highest possible optical purity of the product, the intermediate stages in the preparation of the ketone were carefully controlled. The methyl ester of *l*-menthylxanthic acid, prepared by the method of Tschugaev (*Ber.*, 1899, **32**, 3333) from *l*-menthol, was obtained in 66% yield: m. p. 39°, $[\alpha]_D^{15°}$ −80·5° in benzene ($c = 2{\cdot}30$). Upon dry distillation at about 200°, the ester gave 80% of the calculated yield of *d*-Δ^3-menthene: b. p. 59—60°/9 mm., $n_D^{15°}$ 1·4570, $[\alpha]_D^{15°}$ +106·6° in ether ($c = 2{\cdot}63$) and +118·6° in alcohol ($c = 1{\cdot}65$). The nitrosochloride was then prepared by the method of Richtmann (*Amer. Chem. J.*, 1896, **18**, 762), the yield being increased to 42% through careful cooling: $[\alpha]_D^{15°}$ +221·0° in benzene ($c = 4{\cdot}57$). When treated with 10% alcoholic potassium hydroxide (*loc. cit.*), this substance furnished 80% of the calculated yield of the oxime of *l*-Δ^4-*p*-menthen-3-one, which was purified by distillation in steam: m. p. 63—64°, $[\alpha]_D^{15°}$ −57·8° in alcohol ($c = 2{\cdot}51$). *l*-Δ^4-Menthen-3-one, prepared in 66% yield by hydrolysing the oxime with hydrochloric acid, was a straw-coloured liquid, b. p. 85—88°/11 mm., $n_D^{14°}$ 1·4765, $\alpha_D^{15°}$ −72·02°, $[\alpha]_D^{15°}$ −78·36°.

Upon hydrogenating the ketone (30 g.) in the usual way at 15°, absorption of hydrogen was well maintained for 4 hours. The product recovered after 7 hours' treatment was, however, still slightly lævorotatory and contained a certain amount of thymol. The fraction distilling at 83—99°/11 mm. was rehydrogenated for 1·5 hours, at a temperature which declined gradually from 30° to 20°. Upon refractionation, the product furnished, in a yield of 43%, a specimen of menthone having b. p. 85·5—87·5°/12 mm., $n_D^{15°}$ 1·4550, $[\alpha]_D^{15°}$ +43·24°.

When the above specimen of menthone was treated successively with melting 90% sulphuric acid and alcoholic sodium ethoxide, the values of $[\alpha]_D^{15°}$ shown by the respective products were +27·22° and +7·95°. The menthone obtained by the hydrogenation of *l*-Δ^4-*p*-menthen-3-one was therefore a mixture of *d-iso*menthone and *l*-menthone, in which the former substance predominated.

The Optically Active neo*Menthylamines.*

Experiments on the Formation of d-neo*Menthylamine.*—1. *l*-Menthone, $[\alpha]_D^{15°}$ −27·50°, when heated with dry ammonium formate

in accordance with Wallach's method (*Annalen*, 1898, **300**, 283), yielded a viscid liquid (b. p. 160—163°/9 mm.), which could only be induced to crystallise with difficulty unless inoculated with crystalline material prepared as in method (2) below. When mixed with concentrated hydrochloric acid, the product gave *formyl*-d-neo*menthylamine hydrochloride*, which crystallised from light petroleum in fine opaque needles, m. p. 75—80°; this derivative was stable in dry air, but underwent rapid decomposition in contact with water. When hydrolysed with hot concentrated hydrochloric acid, the viscid product of the original reaction gave a specimen of crude menthylamine hydrochloride having $[\alpha]_D^{15°}$ +5·5° in water; neglecting the possible presence of other isomerides, the product thus appeared to consist of about 28% of *l*-menthylamine hydrochloride in admixture with 72% of *d-neo*menthylamine hydrochloride. When fractionally recrystallised from ethyl acetate, the first fraction had $[\alpha]_D^{15°}$ +8·8° in dilute aqueous solution, but the preparation of pure *d-neo*menthylamine hydrochloride from such a mixture was difficult.

2. Crystalline formyl-*d-neo*menthylamine was obtained more easily by using "inverted *l*-menthone," having $[\alpha]_D^{15°}$ +25·5°, in place of *l*-menthone. After the ketone had been heated for 48 hours with dry ammonium formate, the oily product was separated while hot from the aqueous layer which had formed. After steam-distilling away the unchanged menthone, the residue was separated and then dried by heating with a little alcohol on the water-bath under diminished pressure. The addition of dry ether to the cold dry residue resulted in the immediate separation of crystals (30%), the remainder of the product being an uncrystallisable syrup; 15 g. of ketone yielded on an average 4·4 g. of crystalline product. After one recrystallisation from ether the formyl-*d-neo*menthylamine was pure. When hydrolysed (*Annalen*, 1893, **276**, 308), it yielded its own weight of *d-neo*menthylamine hydrochloride, having $[\alpha]_D^{15°}$ +20·1° in water ($c = 1{\cdot}44$); this value rose to +21·5° after fractional recrystallisation from water.

3. *d-iso*Menthone (7·2 g.), having $[\alpha]_D^{15°}$ +63·4°, was heated with dry ammonium formate (9 g.) for 45 hours. Unchanged menthone was removed by steam distillation, and after extraction with chloroform the formyl derivative was distilled under diminished pressure (6·1 g.; b. p. 170°/15 mm.). The crystalline material obtained by the addition of ether (1 g.) was identical with formyl-*d-neo*menthylamine produced as indicated above.

Characterisation of d-neo*Menthylamine*.—The following observations were made, and for purposes of comparison the corresponding constants noted by Wallach (*Annalen*, 1893, **276**, 306) for "R·

menthylamine" are appended in square brackets. Free *d-neo*menthylamine, $[\alpha]_D^{20°}$ +15·73° [+14·71°]; acetyl-*d-neo*menthylamine, m. p. 169—170°, $[\alpha]_D^{15°}$ +53·0° in chloroform ($c = 1·20$) [168—169°, +50·57°]; benzoyl-*d-neo*menthylamine, m. p. 121·5°, $[\alpha]_D^{15°}$ +22·7° in chloroform ($c = 2·02$) (compare J., 1904, **85**, 68); benzylidene-*d-neo*menthylamine, m. p. 45—46°, $[\alpha]_D^{15°}$ +61·7° in chloroform ($c = 1·56$) [42—43°]; salicylidene-*d-neo*menthylamine m. p. 99—100°, $[\alpha]_D^{15°}$ +30·0° in chloroform ($c = 1·50$) [96—97°]. *β-Naphthalenesulphonyl*-d-neo*menthylamine*, $C_{10}H_{19}·NH·SO_2·C_{10}H_7$, is deposited from alcohol containing a little chloroform in colourless leaflets, m. p. 208°, $[\alpha]_D^{15°}$ +43·7° in chloroform ($c = 2·02$).

The formyl derivative and the hydrochloride of this base, which are particularly distinctive, have been characterised in greater detail. *Formyl*-d-neo*menthylamine*, $C_{10}H_{19}·NH·COH$, melts at 117—118° and has $[\alpha]_D^{15°}$ +53·8° in chloroform ($c = 1·76$) and +62·4° in alcohol ($c = 1·53$) [117·5°, +54·11°]. It is moderately easily soluble in warm ether or light petroleum, but it is most conveniently crystallised from methyl alcohol. Crystals prepared in this way have been examined by Dr. T. V. Barker, of the Department of Mineralogy, University of Oxford, to whose courtesy we owe the following description:

"The crystals belong to the orthorhombic system. Although optically active in solution, they exhibit no hemihedral facets, the holohedral forms being *o*(111), *m*(110) and *q*(011) in the proportions shown in Fig. 1. The axial ratios, $a : b : c = 0·8566 : 1 : 0·7246$, were computed from the following mean results of measurement of two crystals:

	m.	*o*.	*q*.
φ	*49° 25′	49° 27′ (−21)	0° 0′
ρ	90 0	*48 5	36 2 (−6)."

d-neo*Menthylamine hydrochloride*, $C_{10}H_{19}·NH_2,HCl$, melts at 189°, and has $[\alpha]_D^{15°}$ +21·50° in water ($c = 1·44$) [189°, +17·2°]. It dissolves readily in warm light petroleum (b. p. 60—80°), from which it separates slowly in large, transparent prisms. Crystals of the substance were kindly measured by Dr. T. V. Barker, who reports as follows:

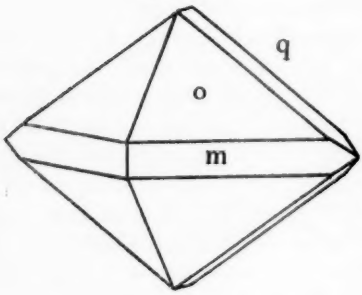
"The crystals belong to the monoclinic system, but exhibit no certain hemihedral character, the forms expressed holohedrally being *b*(010), *m*(110), *a*(100), *s*(021), *q*(011), and, rarely, *o*(1̄11), as shown in Fig. 2. The elements, $a : b : c = 0·3512 : 1 : 0·3430$, $\beta = 100°49′$, were computed from the following mean results of measurements of three crystals:

	b.	*m*.	*a*.	*s*.	*q*.	*o*.
φ	Polar	0° 0′	0° 0′	*79° 11′	*79° 11′	129° 7′ (−10)
ρ	face.	*70 58	90 0	*56 2	*71 23	75 3 (1)

"There is a poor *b*-cleavage. Optically, the negative acute bisectrix is normal to *b* with a wide axial angle. The third mean line makes an angle −15° with the vertical."

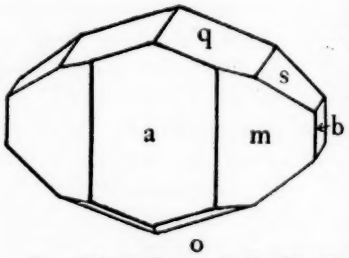
*d-neo*Menthylamine hydrochloride was treated in aqueous solution with the calculated quantity of sodium nitrite solution at 70° (*Annalen*, 1898, **300**, 285); the resulting oil distilled completely at 61°/12 mm., had $n_D^{15°}$ 1·4555, $[\alpha]_D^{15°}$ +58·6° in ether ($c = 1·79$), and appeared to consist of partly racemised *d*-Δ^3-menthene.

FIG. 1.



Formyl-d-neo*menthylamine.*

FIG. 2.



d-neo*Menthylamine hydrochloride.*

l-neo*Menthylamine.*—A specimen of *l-iso*menthone (13·5 g.), having $[\alpha]_D^{15°}$ −37·0°, and prepared from *d*-piperitone by catalytic hydrogenation followed by partial equilibration, when heated in the usual way with ammonium formate yielded a viscid syrup consisting mainly of a mixture of the formyl derivatives of *l-neo*-menthylamine and *d*-menthylamine. Crystallisation of the dry crude material was induced by nucleating it with formyl-*d-neo*-menthylamine in presence of dry ether. The resulting crystals of *formyl*-l-neo*menthylamine* (2·5 g.), after recrystallisation from absolute alcohol, melted at 116—117° and had $[\alpha]_D^{15°}$ −53·6° in chloroform ($c = 1·79$). The substance is thus enantiomorphous with formyl-*d-neo*menthylamine described above, and is of particular interest as the first derivative of *l-neo*menthylamine to be prepared.

Formyl-dl-neo*menthylamine*, prepared by mixing ether solutions of the two enantiomers, melted at 86°. Similar mixtures containing 89, 76, 66, 55, and 24% of formyl-*d-neo*menthylamine melted at 110—114°, 102—104°, 95·5—97·5°, 87—89°, and 103—105°, respectively. The character of the corresponding melting-point curve suggests that an equimolecular mixture of the two enantiomers forms a conglomerate (Roozeboom, *Z. physikal. Chem.*, 1899, **28**, 507).

The Optically Active iso*Menthylamines.*

Experiments on the Formation of d-iso*Menthylamine.*—1. The oxime prepared in good yield from *l*-menthone by treatment for several days with hydroxylamine acetate in aqueous alcohol at the ordinary temperature appeared to be homogeneous; the resulting needles, some of which exceeded 5 cm. in length, melted at 58° and had $[\alpha]_D^{15°}$ −39·7° in absolute alcohol ($c = 1·89$). When reduced with sodium and alcohol (*Annalen*, 1893, **276**, 360), the oxime furnished its own weight of crude *l*-menthylamine hydrochloride, having $[\alpha]_D^{15°}$ −32·6° in water ($c = 1·97$); this value rose to −35·8° after one recrystallisation from water. From this result, the crude product would appear to contain not more than 6·7% of *d-iso*menthylamine hydrochloride, assuming other isomerides to be absent. When treated with nitrous acid, the purified product yielded *l*-menthol, together with some *d*-Δ^3-menthene.

2. When a specimen of "inverted *l*-menthone," having $[\alpha]_D^{15°}$ +19·0°, was treated with hydroxylamine acetate for 6 hours on the water-bath (compare J., 1922, **121**, 586), it gave a 73% yield of a viscid oily oxime, having $[\alpha]_D^{15°}$ −14·3° in alcohol ($c = 1·93$). The derived menthylamine hydrochloride had $[\alpha]_D^{15°}$ −12·5° in aqueous solution, corresponding, in the absence of other isomerides, to a mixture of about 60% of *l*-menthylamine hydrochloride with 40% of *d-iso*menthylamine hydrochloride. After recrystallisation from water, a first fraction showed $[\alpha]_D^{15°}$ −19·2°, indicative of an increased content of *l*-menthylamine hydrochloride, and a similar result attended the use of ethyl acetate as a solvent. The fractional crystallisation of this mixture of hydrochlorides is therefore unsuitable for the ready preparation of pure *d-iso*menthylamine.

3. d-iso*Menthoneoxime*, $C_{10}H_{18}{:}NOH$, was prepared from *d-iso*menthone, having $[\alpha]_D^{15°}$ +65·7° and obtained by hydrogenating *l*-piperitone. The ketone was mixed in aqueous alcoholic solution with hydroxylamine acetate and kept at the ordinary temperature for 3 days. Most of the alcohol was distilled off, and the product worked up in the usual way (*loc. cit.*). The oxime was isolated in 86% yield, as a viscid oil which could not be induced to crystallise from any of the ordinary organic solvents. Cooling in a freezing mixture and prolonged keeping in a vacuum over concentrated sulphuric acid were also without effect in this respect. The oxime had $[\alpha]_D^{15°}$ +46·0° in absolute alcohol ($c = 1·67$), and $n_D^{15°}$ 1·4845.

d-iso*Menthylamine Hydrochloride*, $C_{10}H_{19}{\cdot}NH_2,HCl$.—When reduced with sodium in alcoholic solution, the above oxime (82 g.) yielded a crude menthylamine hydrochloride having $[\alpha]_D^{15°}$ +20·63° in aqueous

solution ($c = 1{\cdot}53$). After one recrystallisation from boiling acetone containing a little methyl alcohol, a fraction (33 %) was obtained having $[\alpha]_D^{15°}$ $+23{\cdot}60°$, and this value was unaffected by further recrystallisation. The pure substance formed clusters of long, silky needles, which did not melt below 250° (Found: Cl, 18·3. $C_{10}H_{21}N,HCl$ requires Cl, 18·5%). The mother-liquors yielded fractions of lower dextrorotation, which have been reserved for further examination.

Characterisation of d-iso*Menthylamine.*—*Formyl*-d-iso*menthylamine*, $C_{10}H_{19}{\cdot}NH{\cdot}COH$, prepared by heating the free base with anhydrous formic acid in a sealed tube at 200° for several hours, is extremely soluble in the ordinary organic solvents. From light petroleum it separates in soft, feathery needles, m. p. 45—46°, $[\alpha]_D^{15°}$ $+31{\cdot}3°$ in chloroform ($c = 1{\cdot}69$). *Acetyl*-d-iso*menthylamine*, $C_{10}H_{19}{\cdot}NH{\cdot}CO{\cdot}CH_3$, forms very soluble, colourless needles, m. p. 77—79°, $[\alpha]_D^{15°}$ $+30{\cdot}7°$ in chloroform ($c = 1{\cdot}96$). *Benzoyl*-d-iso*menthylamine*, $C_{10}H_{19}{\cdot}NH{\cdot}COPh$, crystallises from acetone, in which it is readily soluble, in coarse needles, m. p. 97—98°, $[\alpha]_D^{15°}$ $+18{\cdot}3°$ in chloroform ($c = 3{\cdot}1$). β-*Naphthalenesulphonyl*-d-iso*menthylamine*, $C_{10}H_{19}{\cdot}NH{\cdot}SO_2{\cdot}C_{10}H_7$, prepared by the Schotten–Baumann method, crystallises from alcohol in large plates, m. p. 80—81°, $[\alpha]_D^{15°}$ $-2{\cdot}8°$ in chloroform ($c = 1{\cdot}80$). *Benzylidene*-d-iso*menthylamine*, $C_{10}H_{19}{\cdot}N{:}CHPh$, separates from methyl alcohol in colourless plates, m. p. 67—68°, $[\alpha]_D^{15°}$ $+90{\cdot}7°$ in chloroform ($c = 1{\cdot}68$). *Salicylidene*-d-iso*menthylamine*, $C_{10}H_{19}{\cdot}N{:}CH{\cdot}C_6H_4{\cdot}OH$, is deposited from alcohol in coarse, yellow needles, m. p. 122°, $[\alpha]_D^{15°}$ $+77{\cdot}6°$ in chloroform ($c = 1{\cdot}80$). d-iso-*Menthylcarbamide*, $C_{10}H_{19}{\cdot}NH{\cdot}CO{\cdot}NH_2$, crystallises from ether–light petroleum in minute, colourless needles, m. p. 141·5—142·5°, $[\alpha]_D^{15°}$ $+29{\cdot}0°$ in chloroform ($c = 1{\cdot}34$). d-iso-*Menthylphenylcarbamide*, $C_{10}H_{19}{\cdot}NH{\cdot}CO{\cdot}NHPh$, separates from methyl alcohol in long, colourless needles, m. p. 142°, $[\alpha]_D^{15}$ $+21{\cdot}8°$ in chloroform ($c = 1{\cdot}38$). d-iso*Menthylphenylthiocarbamide*, $C_{10}H_{19}{\cdot}NH{\cdot}CS{\cdot}NHPh$, crystallises from light petroleum containing a little alcohol in colourless needles, m. p. 114·5—115·5°, $[\alpha]_D^{15°}$ $+46{\cdot}7°$ in chloroform ($c = 1{\cdot}33$). All these derivatives were readily obtained pure, thus indicating the homogeneity of the original base.

Upon treatment with nitrous acid, *d-iso*menthylamine yielded a crystalline dextrorotatory *iso*menthol, the characteristics of which will be described in a later communication.

l-iso*Menthylamine.*—Upon oximation in the manner described above for *d-iso*menthone, a specimen of *l-iso*menthone having $[\alpha]_D^{15°}$ $-71{\cdot}41°$ yielded *l*-iso*menthoneoxime* as a viscid oil, with $n_D^{15°}$ 1·4870 and $[\alpha]_D^{15°}$ $-45{\cdot}2°$ in absolute alcohol ($c = 1{\cdot}93$). Upon reduction with sodium and alcohol, this gave crystalline l-iso*menthyl-*

amine hydrochloride, having $[\alpha]_D^{15°}$ −19·1° in water (c = 2·77). When recrystallised from boiling acetone containing a little methyl alcohol, the crude hydrochloride yielded a first fraction (20%) having $[\alpha]_D^{15°}$ −21·88° in water. *Salicylidene*-l-iso*menthylamine* crystallises from alcohol in coarse, yellow needles, m. p. 122°, $[\alpha]_D^{15°}$ −76·8° in chloroform (c = 1·72). The base is therefore proved to be enantiomorphous with the preceding *d-iso*menthylamine.

Salicylidene-dl-iso*menthylamine*, prepared by mixing equal weights of the *d*- and *l*-components in alcohol, melted at 95°.

The authors are indebted to the Carnegie Trust for a Teaching Fellowship which enabled one of them (Dr. Robertson) to take part in the work. The investigations are being continued; a cognate research is also in hand, dealing with the corresponding relationships of the carvomenthones.

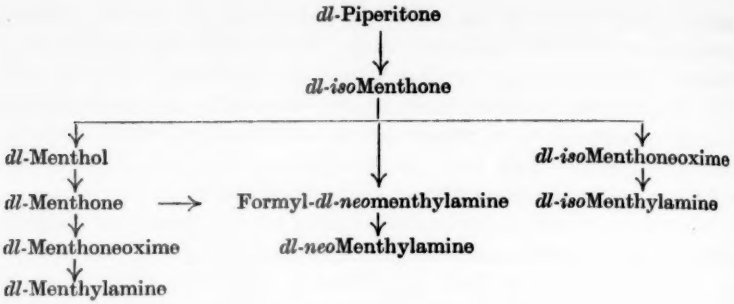
UNITED COLLEGE OF ST. SALVATOR AND ST. LEONARD,
UNIVERSITY OF ST. ANDREWS. [*Received, June 10th*, 1926.]

CCXCIV.—*Researches in the Menthone Series. Part III. Optically Inactive Menthylamines.*

By JOHN READ, ALISON MARY RITCHIE COOK, and (in part) MARY ISOBEL SHANNON.

THIS communication deals mainly with the preparation and characterisation of *dl*-menthylamine, *dl-neo*menthylamine, and *dl-iso*menthylamine. Up to the present, the only definite data available concerning externally compensated menthylamines would appear to be contained in Wallach's description of a so-called "i-Menthylamine," and certain of its derivatives, prepared by the reduction of *dl*-menthoneoxime (*Annalen*, 1913, **397**, 218). As shown below, these derivatives are to be regarded as characteristic of *dl-iso*menthylamine rather than of *dl*-menthylamine.

The utilisation of *dl*-piperitone as a starting point for the preparation of the three stereoisomeric optically inactive menthylamines in question follows from an application of the methods which have been laid down in the two preceding communications of this series (J., 1925, **127**, 2782; this vol., p. 2210). It may therefore be sufficient to indicate the scheme of operations briefly by means of a diagrammatic summary:



In all three instances homogeneous products were isolated without difficulty. The three optically inactive bases give rise to distinctive series of derivatives, the majority of which may be readily obtained crystalline. A broad resemblance may be traced between *dl*-menthylamine and *dl-iso*menthylamine, whilst *dl-neo*menthylamine presents certain unique features. Thus, the hydrochlorides of the first two bases are practically insoluble in ether and do not melt below 250°; *dl-neo*menthylamine hydrochloride, however, dissolves readily in ether, and even in light petroleum, and melts at 184—185°. This base is also characterised by the beauty of its crystalline derivatives: thus, it has been possible to submit both the externally compensated and the optically active hydrochloride and formyl derivative of the *neo*-base to goniometric examination, with results of considerable interest. Such similarities and differences between the bases accord satisfactorily with the relative molecular configurations recently advanced for them (this vol., p. 2213), in which menthylamine and *iso*menthylamine differ only in the asymmetry of carbon atom (1). A similar resemblance is to be anticipated between *neo*menthylamine and the still unknown *neoiso*menthylamine, which, in accordance with the scheme indicated, display a corresponding configurational relationship.

With certain exceptions, including most of the carbamide derivatives, the externally compensated derivatives of all three bases possess lower melting points than their optically active components. In view of the unusually interesting stereochemical relationships existing between the three optically inactive and six optically active menthylamines which are now readily available, starting from *dl*-, *d*-, and *l*-piperitone, we propose to undertake further studies of these bases and their derivatives, including a complete investigation of the optical resolution of the externally compensated forms. It is hoped also to prepare *neoiso*menthylamine, possibly by a suitable application of the Walden inversion. For the present, the appended summary of melting points and specific rotatory powers affords a

comprehensive survey of some of the most important derivatives of the three bases now known. The values of $[\alpha]_D$, denoted by the prefixed + or − signs, were observed in water for the hydrochlorides and in chloroform for the remaining derivatives (this vol., pp. 2219, 2222):

	Menthylamines.		*neo*Menthylamines.		*iso*Menthylamines.	
Derivative.	*dl*-.	*l*-.	*dl*-.	*d*-.	*dl*-.	*d*-.
Hydrochloride.	>250°	>280° *	184—185°	189°	>250°	>250°
		−36·6°†		+21·5°		+23·6*
Formyl.	77—78	102—103*	86	117—118	45—47	45—46
		−83·8*		+53·8		+31·3
Acetyl.	123—124	145*	160—161	169—170	Liquid	77—79
		−81·7*		+53·0		+30·7
Benzoyl.	145—146	157	101—102	121·5	127—128	97—98
		−62·8		+22·7		+18·3
β-Naphthalene-sulphonyl.	145—146	135	209—210	208	141—142	80—81
		−53·3		+43·7		−2·8
Benzylidene.	Liquid	69—70	Liquid	45—46	41—44	67—68
		−132·5		+61·7		+90·7
Salicylidene.	Liquid	57—58	69·5	99—100	95	122
		−119·2		+30·0		+77·6
Carbamide.	157	134—136*	162—163	155—156*	203—204	141·5—142·5
						+29·0
Phenylcarbamide.	162	140—141*	183—184	177—178*	142—143	142
						+21·8
Phenylthiocarbamide.	151	135*	169—170	178—179*	137	114·5—115·5
						+46·7

* Wallach, *Annalen*, 1893, **276**, 306; 1898, **300**, 278.
† Tutin and Kipping, J., 1904, **85**, 65.

The tabulated constants show the importance of selecting suitable derivatives in diagnosing a particular menthylamine, as the values for the same derivative of two stereoisomerides are in some instances almost identical.

It may now be pointed out that Wallach's "i-Menthylamine" (*loc. cit.*), since it is stated to have been prepared by reducing *dl*-menthoneoxime, would be expected to yield derivatives possessing the properties recorded in the second column of the above table. Apart from the hydrochloride, which cannot easily be used in discriminating between *dl*-menthylamine and *dl-iso*menthylamine, the carbamide (m. p. 151—152°) is the sole derivative which fulfils this condition even approximately. The phenylcarbamide (m. p. 135—136°) and the phenylthiocarbamide (m. p. 136—137°) melt at practically the same temperatures as the corresponding *dl-iso*-menthylamine derivatives, whilst the melting point, 141—142°, quoted for the benzylidene derivative is perhaps a misrendering of 41—42°. It would thus appear, as suggested in another connexion (J., 1925, **127**, 2783), that Wallach's "inactive menthone" consisted of *dl-iso*menthone, which upon oximation in an alkaline medium would yield a mixture of *dl-iso*menthoneoxime and *dl*-menthoneoxime.

The need for a careful observance of the experimental conditions adopted in preparing the various stereoisomeric menthylamines and related substances is emphasised further by the results of attempts to

utilise *dl*-piperitoneoxime as a source of optically inactive menthylamines. These experiments, which were conducted prior to the successful operations outlined above, although affording no useful method of preparing pure menthylamines, are of considerable interest as suggesting a possible line of approach from piperitone to piperitylamine and piperitol.

Experimental.

Preparation and Characterisation of dl-*Menthylamine.*—*dl*-Menthoneoxime (10 g.; m. p. 81—82°), prepared from *dl*-piperitone via *dl-iso*menthone, *dl*-menthol, and *dl*-menthone (J., 1925, **127**, 2782), was dissolved in absolute alcohol (75 c.c.) and reduced with metallic sodium (15 g.) on a boiling water-bath, further quantities of absolute alcohol (60 c.c.) being added as needed, in order to effect the complete solution of the sodium. Upon steam distilling the product and evaporating the distillate to dryness with dilute hydrochloric acid, crude, crystalline dl-*menthylamine hydrochloride* was obtained in almost theoretical yield. Upon recrystallisation from boiling acetone containing a little methyl alcohol, it separated in small, glistening needles, which did not melt below 250° (Found: Cl, 18·4. $C_{10}H_{21}N,HCl$ requires Cl, 18·5%). The substance dissolves sparingly in boiling acetone or ethyl acetate, and readily in alcohol or water; it is practically insoluble in ether or light petroleum. The crude product of the reduction appeared to be substantially homogeneous, but in preparing derivatives the hydrochloride was recrystallised twice before use.

dl-*Menthylamine chloroplatinate* crystallises from hot water in small, deep orange prisms, m. p. 201—202° (decomp.). The *picrate* is deposited from warm alcohol in well-defined, transparent, pale yellow prisms, m. p. 196—198°. Free dl-*menthylamine* is a liquid which resembles *l*-menthylamine closely in its odour and general properties.

The *formyl* derivative was prepared by heating the free base with an excess of anhydrous formic acid in a sealed tube at 200° for 5 hours. It crystallises from light petroleum in clusters of minute, glistening prisms, m. p. 77—78°. *Acetyl*-dl-*menthylamine*, prepared by the interaction of the free base and acetic anhydride in dry ether, separates from ether–light petroleum in long, silky needles, m. p. 123—124°. *Benzoyl*-dl-*menthylamine*, obtained by the Schotten–Baumann reaction, is deposited from methyl alcohol in elongated, transparent prisms, m. p. 145—146°. β-*Naphthalenesulphonyl*-dl-*menthylamine*, prepared similarly, crystallises from methyl alcohol in clusters of small, transparent prisms, m. p. 145—146°. *Benzylidene*-dl-*menthylamine* was readily produced by mixing the free base

and benzaldehyde in ether; it forms a colourless oil at the ordinary temperature. *Salicylidene*-dl-*menthylamine*, prepared similarly, is a pale yellow oil.

dl-*Menthylcarbamide* separated as an oil upon mixing *dl*-menthylamine hydrochloride and potassium cyanate in aqueous solution; it crystallised slowly when kept, and was deposited from acetone in soft, opaque needles, m. p. 157°.

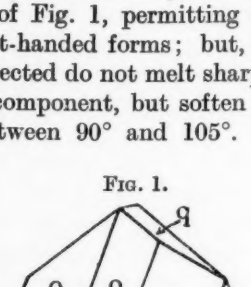
dl-*Menthylphenylcarbamide*, made by mixing the free base and phenylcarbimide in dry ether, was deposited from methyl alcohol in soft needles, m. p. 162°. dl-*Menthylphenylthiocarbamide*, prepared in an analogous manner, crystallised from methyl alcohol in small, lustrous, elongated prisms, m. p. 151°.

Action of nitrous acid on dl-*menthylamine*. Upon treating an aqueous solution of *dl*-menthylamine hydrochloride (5 g.) with the calculated amount of sodium nitrite solution, added drop by drop at 70°, effervescence occurred and an oil was produced. This was removed by steam distillation, extracted with ether, and dried over anhydrous sodium sulphate. Upon distillation, most of the product passed over at 104—107°/20 mm.; the distillate had $n_D^{16°}$ 1·4600 and consisted of *dl*-menthol and *dl*-Δ^3-menthene.

Preparation and Characterisation of dl-neo*Menthylamine*.—The product obtained by heating *dl-iso*menthone with ammonium formate (compare *Annalen*, 1898, **300**, 283; this vol., p. 2217) was freed from unchanged ketone by steam distillation; the residual crude formyl derivative was then extracted with ether and distilled under diminished pressure. The fraction distilling at 160—170°/10 mm. crystallised partly when kept for several days. The crystalline material was separated from the accompanying viscid syrup by filtration with suction, followed by treatment on porous plate and recrystallisation from light petroleum–ether. The resulting pure *formyl*-dl-neo*menthylamine*, $C_{10}H_{19}\cdot NH\cdot COH$, formed large, transparent prisms, m. p. 86°, the average yield being about 20% of the crude product. *dl*-Menthone furnished the same substance when treated similarly. Formyl-*dl-neo*menthylamine dissolves readily in most of the common organic solvents, and is considerably more soluble than formyl-*d-neo*menthylamine (this vol., p. 2219); from light petroleum, in which it is only moderately easily soluble, it separates in fine needles attaining a length of 3 cm. Slow deposition from light petroleum–ether usually results in the formation of compact prisms, although the needles often appear towards the end of the crystallisation. No difference in melting point was observed between the two forms. The appended crystallographic description has been kindly supplied by Dr. T. V. Barker, of the Department of Mineralogy, University of Oxford:

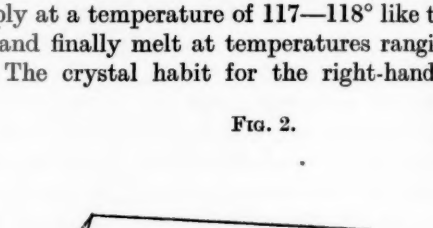
" The substance is dimorphous. One form is orthorhombic and exhibits a close similarity to the *d*-component previously described (this vol., p. 2219). It is therefore either a conglomerate or a pseudo-racemic substance; and although the character of the melting-point curve favours the former possibility (this vol., p. 2220), the evidence in another direction is somewhat inconclusive. On the one hand, the crystals exhibit well-developed hemihedral facets, *x* of Fig. 1, permitting a mechanical segregation into right- and left-handed forms; but, on the other hand, individual crystals so selected do not melt sharply at a temperature of 117—118° like the *d*-component, but soften and finally melt at temperatures ranging between 90° and 105°. The crystal habit for the right-handed

FIG. 1.



Formyl-dl-neo*menthylamine.*

FIG. 2.



dl-neo*Menthylamine hydrochloride.*

variety (geometrically) is given in Fig. 1, the list of forms being *b*(010), *m*(110), *q*(0$\bar{1}$1), together with *o*(111) developed holohedrally and *x*(121) hemihedrally. The inverse form *x*′(1$\bar{2}$1) is of course exhibited by the left-handed variety. The axial ratios, $a : b : c = 0{\cdot}8506 : 1 : 0{\cdot}7208$, were derived from the following results of measurement of four crystals (two of each kind) :

	b.	*m*.	*o*.	*x*.	*q*.
ϕ	0° 0′	*49° 37′	49° 44′ (−7)	30° 29′ (−2)	0° 0′
ρ	90 0	90 0	*48 3	59 13 (−6)	35 58 (−11)

" Optically, the axial plane is *b*(010) and the positive acute bisectrix is normal to *a*(100). The axial angle for red is considerably greater than for violet.

" The second form is acicular and optically different from the first form, since, although the sign of the double refraction is again positive, the axial angle for red light is less than that for violet.

The needles have a positive elongation optically, and the axial plane is transverse."

A large single crystal of the substance, weighing about 0·2 g., showed a slight but distinct dextrorotation when dissolved in absolute alcohol. The melting point of the substance prepared as above was the same as that of an equimolecular mixture of formyl-*d*-*neo*menthylamine and formyl-*l*-*neo*menthylamine, prepared as described in an earlier communication (this vol., p. 2220).

When hydrolysed with boiling concentrated hydrochloric acid (*Annalen*, 1893, **276**, 308), formyl-*dl*-*neo*menthylamine yielded about its own weight of dl-neo*menthylamine hydrochloride*, $C_{10}H_{19}\cdot NH_2,HCl$. This substance dissolves readily in most of the common organic solvents, including light petroleum, but it is less soluble than the externally compensated compound. When dissolved in warm light petroleum, it is obtained on slow deposition at the ordinary temperature in large, transparent crystals, m. p. 184—185° (Found: Cl, 18·4. $C_{10}H_{21}N,HCl$ requires Cl, 18·5%). The preparation appeared to be homogeneous. Crystals of this substance were kindly examined by Dr. T. V. Barker, who reports as follows:

"The crystals of *dl*-*neo*menthylamine hydrochloride show no resemblance to those of the *d*-component previously described (this vol., p. 2219), and accordingly represent a truly racemic substance. The system is monoclinic, the forms exhibited being *r*(101), *t*($\bar{3}$01), *o*(111) and *p*($\bar{1}$11) as illustrated by Fig. 2. The two crops examined were not very suitable for measurement, so the elements, $a:b:c = 3{\cdot}367:1:1{\cdot}652$, $\beta = 92°\,39'$, are not very accurate. Following are the mean results of measurement of four crystals, reduced in terms of a hypothetical vertical zone:

	o.	*r*.	*p*.	*s*.
ϕ	61° 45′	61° 45′	*113° 59′	*144° 59′
ρ	*34 30	90 0	34 0 (−32)	90 0

"Optically, negative; the axial plane is *b*(010), one optic axis making an angle of about + 20° with the vertical."

A large single crystal, weighing about 0·3 g., showed no optical activity when dissolved in water.

dl-neo*Menthylamine chloroplatinate* crystallises from water in minute, orange prisms, m. p. 206—207° (decomp.); it is more soluble in water than the corresponding derivatives of *dl*-menthylamine and *dl*-*iso*menthylamine. The *hydrobromide* crystallises from alcohol in lustrous, elongated prisms and does not melt below 220°. It dissolves only sparingly in ether and is practically insoluble in light petroleum. The *picrate* crystallises from alcohol in orange prisms or lustrous, yellow needles, m. p. 183—184°; the dimorphism is less pronounced than in the case of *dl*-*iso*menthylamine picrate. Free

dl-neo*menthylamine* is a liquid with an odour closely resembling that of *l*-menthylamine; the physical constants have not yet been determined.

Acetyl-dl-neo*menthylamine* crystallises from light petroleum–ether in fine, silky needles, m. p. 160—161°. *Benzoyl*-dl-neo*menthylamine* crystallises from light petroleum in long, glistening needles, m. p. 101—102°. β-*Naphthalenesulphonyl*-dl-neo-*menthylamine* is sparingly soluble in boiling methyl alcohol, from which it separates in small, glistening plates, m. p. 209—210°. *Benzylidene*-dl-neo*menthylamine* is a colourless oil at the ordinary temperature, but it crystallises when immersed in a freezing mixture. *Salicylidene*-dl-neo*menthylamine* crystallises from methyl alcohol in stout, yellow needles, m. p. 69·5° (Found: C, 79·2; H, 9·3. $C_{17}H_{25}ON$ requires C, 78·8; H, 9·3%).

dl-neo*Menthylcarbamide* separated in the crystalline condition upon mixing aqueous solutions of *dl-neo*menthylamine hydrochloride and potassium cyanate; upon recrystallisation from acetone it formed transparent, elongated prisms, m. p. 162—163°, which became opaque when kept for a few days. dl-neo*Menthylphenylcarbamide* separated from methyl alcohol in elongated, transparent prisms, capable of goniometric measurement, m. p. 183—184°. dl-neo*Menthylphenylthiocarbamide* crystallised from methyl alcohol in small, transparent prisms, m. p. 169—170°.

All the above derivatives were made from recrystallised *dl-neo*menthylamine hydrochloride; they were obtained pure without difficulty, and appeared to be homogeneous.

Action of nitrous acid on dl-neo*menthylamine.* Upon treatment with nitrous acid in the way described above, *dl-neo*menthylamine hydrochloride (5 g.) yielded a colourless oil, the bulk of which distilled at 130° under atmospheric pressure; the distillate had $n_D^{16°}$ 1·4550, and appeared to consist essentially of *dl*-Δ^3-menthene.

Preparation and Characterisation of dl-iso*Menthylamine.—dl*-Piperitone was converted to *dl-iso*menthone by successive treatment with (*a*) sodium and alcohol and (*b*) chromic acid, crystalline *dl-iso*menthoneoxime being then prepared in the manner indicated in a former communication (J., 1925, **127**, 2782). The pure oxime (m. p. 99—100°), upon reduction with sodium and absolute alcohol in the manner described above for *dl*-menthoneoxime, furnished an almost theoretical yield of the crude crystalline hydrochloride of *dl-iso*menthylamine. Repeated recrystallisation from acetone indicated the substantial homogeneity of the product.

dl-iso*Menthylamine hydrochloride* dissolves readily in water or alcohol, but is practically insoluble in ether or light petroleum. It is moderately easily soluble in boiling acetone containing a little

methyl alcohol, from which it crystallises in small, glistening needles which do not melt below 250° (Found: Cl, 18·6. $C_{10}H_{21}N,HCl$ requires Cl, 18·5%). The viscid mother-liquor from crystalline *dl-iso*menthoneoxime (*loc. cit.*) also furnished a crystalline hydrochloride when treated as outlined above; when recrystallised twice from boiling acetone containing a little methyl alcohol, this product yielded a fraction which appeared to consist of pure *dl-iso*menthylamine hydrochloride, since it readily gave rise to identical derivatives (Found: Cl, 18·4%).

dl-iso*Menthylamine chloroplatinate* crystallises from water in pale orange needles, m. p. 212—213° (decomp.). The *picrate* exhibits dimorphism when crystallised from boiling water containing a little methyl alcohol, forming either feathery, orange needles or elongated, pale yellow prisms, m. p. 171—173°. Free dl-iso*menthylamine* resembles *l*-menthylamine in odour; its physical constants will be reported later.

Formyl-dl-iso*menthylamine* is distinguished by its great solubility in organic solvents, including light petroleum, from which it crystallises in soft needles, m. p. 45—47°. *Acetyl*-dl-iso*menthylamine* is a colourless oil, which dissolves readily in the ordinary organic solvents; it crystallises only when cooled in a freezing mixture. *Benzoyl*-dl-iso*menthylamine* crystallises from acetone in soft, glistening needles m. p. 127—128°. A recrystallised specimen of menthylamine hydrochloride obtained by reducing the syrupy mother-liquor from *dl-iso*menthoneoxime yielded a mixed product (4·7 g.) upon benzoylation. A small fraction (0·5 g.) which remained undissolved after treatment with ether was deposited from methyl alcohol in colourless needles, m. p. 184°, and was found to be identical with a benzoylmenthylamine obtained from *dl*-piperitoneoxime (*vide infra*). The ether extract furnished fractions melting indefinitely at temperatures between 115° and 145°. β-*Naphthalenesulphonyl*-dl-iso*menthylamine* crystallises from methyl alcohol in small needles, m. p. 141—142°. *Benzylidene*-dl-iso*menthylamine* is very soluble in organic solvents; it separates from methyl alcohol in radial aggregates of small, glistening prisms, m. p. 41—44°. *Salicylidene*-dl-iso*menthylamine* crystallised from methyl alcohol in yellow, elongated prisms, m. p. 95°; it was identical with the derivative made by mixing equal quantities of salicylidene-*d-iso*menthylamine and salicylidene-*l-iso*menthylamine, as described in a previous communication (this vol., p. 2223).

dl-iso*Menthylcarbamide* separated as a crystalline product when prepared in the usual way; it was deposited from acetone containing a little methyl alcohol in small, glistening needles, m. p. 203—204°. dl-iso*Menthylphenylcarbamide* crystallises from methyl alcohol in

transparent plates, m. p. 142—143° (Found : C, 74·2; H, 9·4. $C_{17}H_{26}ON_2$ requires C, 74·5; H, 9·4%). dl-iso*Menthylphenylthiocarbamide* crystallises from methyl alcohol in small, hard prisms, m. p. 137°.

Action of nitrous acid on dl-iso*menthylamine.* When treated with nitrous acid in the usual way, *dl-iso*menthylamine hydrochloride yielded a dl-iso*menthol*, crystallising in fine needles, m. p. 51—53°. Further quantities of this substance are being accumulated for the purpose of detailed characterisation.

The Reduction of Piperitoneoxime.—As an outcome of a series of somewhat tedious experiments carried out by Miss M. I. Shannon, B.Sc., Ph.D., it was found possible to isolate small amounts of some of the above derivatives of *dl-iso*menthylamine from the mixture of bases obtained by reducing *dl*-piperitoneoxime. The crystalline mixture of α- and β-oximes (J., 1922, **121**, 582) obtained from racemised piperitone (J., 1923, **123**, 2270) was reduced in small quantities (20 g.) in absolute alcohol (200 c.c.) by means of metallic sodium (40 g.) in the manner adopted for the menthoneoximes, further quantities of absolute alcohol (160 to 200 c.c.) being added at intervals in order to prevent the separation of solid sodium ethoxide. The resulting base was removed by steam distillation and evaporated to dryness on the water-bath with dilute hydrochloric acid : on an average, 20 g. of oxime yielded about 19 g. of crystalline hydrochloride. The product dissolved sparingly in light petroleum, moderately in warm ether, readily in boiling ethyl acetate, and freely in chloroform, benzene, acetone, alcohol, or water. For further work, it was recrystallised from hot ethyl acetate, from which it separated in small, glistening needles, m. p. 258—260° (decomp.) (Found : Cl, 18·6. $C_{10}H_{21}N,HCl$ requires Cl, 18·5%. $C_{10}H_{19}N,HCl$ requires Cl, 18·7%). Unsuccessful attempts were made to effect a more complete separation of the bases by fractionally crystallising the derived sulphate mixture, which was less soluble in organic solvents than the hydrochloride.

The free base isolated from the above recrystallised hydrochloride resembled the menthylamines closely in its ordinary characteristics. It distilled under atmospheric pressure in a current of hydrogen at 190—193°, and absorbed carbon dioxide from the air, forming a solid carbonate. The chloroplatinate gave a sparingly soluble fraction, crystallising from hot water in pale orange needles, m. p. 209—210° (Found : Pt, 27·1. $C_{20}H_{44}N_2Cl_6Pt$ requires Pt, 27·1%). The first fraction of the picrate (60 g.) separated from hot water in lustrous, yellow plates, m. p. 152—153°; the melting point remained unaltered after several recrystallisations, but the mother-liquor yielded a small quantity of acicular crystals melting rather indefinitely at

about 130°. The crude benzoate (1·1 g.) melted indefinitely at about 134°, but after five recrystallisations from hot water a homogeneous fraction (0·2 g.), m. p. 182—183°, was obtained in fine, soft needles.

The crude benzoyl derivative (6 g.) when recrystallised four times from methyl alcohol yielded a small quantity (0·3 g.) of colourless needles, m. p. 184°; the melting point was unaffected by further recrystallisation, and the analysis corresponded to a benzoylmenthylamine (Found: C, 79·3; H, 9·7. $C_{17}H_{25}ON$ requires C, 78·8; H, 9·7%). Unlike the benzoate, this derivative was insoluble in hot water. The mother-liquors furnished fractions with lower and indefinite melting points. After repeated recrystallisation from light petroleum, followed by methyl alcohol, the crude *p*-toluenesulphonyl derivative gave a small fraction consisting of fine needles, m. p. 142—143°, the melting point being unaffected by further recrystallisation.

The crude salicylidene derivative (6·7 g.) after four recrystallisations from methyl alcohol gave a small fraction (0·25 g.) consisting of pale yellow, glistening needles, m. p. 93—94°. The crude piperonylidene derivative after repeated recrystallisation from methyl alcohol–ether gave a small fraction of fine needles melting very definitely at 235—236°.

The carbamide (2·5 g.) separated as an oil which became partly crystalline after keeping for several weeks. Repeated treatment with dry ether, followed by recrystallisation from warm acetone, furnished a small quantity (0·25 g.) of lustrous, silky needles, m. p. 179—180°; the melting point was unaffected by further recrystallisation. The crude phenylthiocarbamide (4·5 g.) after four recrystallisations from methyl alcohol yielded a small quantity (1 g.) of colourless prisms, m. p. 135—136°. Efforts to prepare a crystalline phenylcarbamide, benzylidene derivative or anisylidene derivative were unsuccessful.

The least soluble components of the chloroplatinate, salicylidene derivative, and phenylthiocarbamide thus melt at practically the same temperatures as the corresponding derivatives of *dl-iso*menthylamine, and their identity was confirmed by means of melting-point mixtures. The benzoyl derivative, m. p. 184°, appeared to be identical with a benzoyl derivative furnished in small amount by the reduction product from the viscid mother-liquor of *dl-iso*menthoneoxime (*vide supra*). The derived picrate, in spite of its unchanged melting point after recrystallisation, cannot be regarded as homogeneous. It may be concluded from the whole series of observations that the reduction of *dl*-piperitoneoxime leads to the formation of a mixture of bases, including *dl-iso*menthylamine.

A study of the action of nitrous acid on the crude hydrochloride (75 g.) indicated the possibility of incomplete reduction, so that some of the substances described above may be derivatives of *dl*-piperitylamine. The product of the reaction was a faintly yellow oil, which after two distillations under diminished pressure yielded the following fractions: (1) b. p. 60—65°/11 mm., $n_D^{15°}$ 1·4622, 6·1 g.; (2) 65—70°/8 mm., 1·4650, 2·5 g.; (3) 70—92°/8 mm., 1·4699, 4·0 g.; (4) 92—94°/10 mm., 1·4708, 8·2 g.; (5) 95—98°/10 mm., 1·4715, 6·0 g.; (6) 98—107°/9 mm., 1·4729, 4·7 g. The first three fractions contained menthene ($n_D^{15°}$ 1·4555) and possibly terpinene, whilst the last three possessed an odour of menthol ($n_D^{20°}$ 1·4642) mingled apparently with that of piperitol ($n_D^{22°}$ 1·4760).

A specimen of *l*-piperitoneoxime having $[\alpha]_D$ + 145·0° in benzene, prepared from *l*-piperitone having $[\alpha]_D$ − 34·0° (J., 1923, **123**, 2271), when reduced in a similar manner yielded a crude hydrochloride having $[\alpha]_D$ + 13·4° in a 1% aqueous solution.

Derivatives of l-*Menthylamine.*—We are indebted to Dr. G. J. Robertson for the following information concerning certain derivatives of *l*-menthylamine which are of interest in connexion with the work now described.

Benzoyl-l-*menthylamine* (compare J., 1904, **85**, 70) crystallises from methyl alcohol in coarse needles, m. p. 157°, $[\alpha]_D$ − 62·8° in chloroform (c = 2·33). *β-Naphthalenesulphonyl*-l-*menthylamine* crystallises from methyl alcohol in long, stout prisms, m. p. 135°, $[\alpha]_D$ − 53·3° in chloroform (c = 2·03). *Benzylidene*-l-*menthylamine* (compare *Annalen*, 1893, **276**, 305) forms coarse needles, m. p. 69—70°, $[\alpha]_D$ − 132·5° in chloroform (c = 1·71). *Salicylidene*-l-*menthylamine* separates from methyl alcohol in coarse needles, m. p. 57—58°, $[\alpha]_D$ − 119·2° in chloroform (c = 1·75).

We express our indebtedness to the Department of Scientific and Industrial Research for a maintenance grant to one of the authors (A.M.R.C.). The investigation is being continued.

UNITED COLLEGE OF ST. SALVATOR AND ST. LEONARD,
UNIVERSITY OF ST. ANDREWS. [*Received, June 16th*, 1926.]

CCXCV.—*The Condensation of Benzyl Methyl Ketone with Salicylaldehyde.*

By ROBERT DICKINSON.

THE condensation of benzyl methyl ketone with benzaldehyde was studied by Goldschmiedt and Knöpfer (*Monatsh.*, 1897, **18**, 437; 1898, **19**, 406) and Goldschmiedt and Krczmar (*ibid.*, 1901,

22, 659). With dilute aqueous sodium hydroxide as condensing agent, the product obtained was a mixture of styryl benzyl ketone and 2 : 3 : 6-triphenyltetrahydro-4-pyrone, together with a very small quantity of $\alpha\gamma\varepsilon$-triphenylacetyl-$\beta\delta$-diphenylpentane. With dry hydrogen chloride as condensing agent, δ-chloro-$\gamma\delta$-diphenylbutan-β-one was obtained which readily lost hydrogen chloride to give $\gamma\delta$-diphenyl-Δ^{γ}-buten-β-one, isomeric with styryl benzyl ketone; when an excess of the ketone was used, the product contained a yellow substance which was regarded as 4 : 5 : 6-triphenyl-3-methyl-Δ^{2}-*cyclo*hexenone, formed according to the equation:

$$\begin{matrix}\mathrm{Ph{\cdot}CH{\cdot}CO{\cdot}CH_3}\\ \mathrm{Ph{\cdot}CH{\cdot}CHPh{\cdot}CO{\cdot}CH_3}\end{matrix} = \begin{matrix}\mathrm{Ph{\cdot}CH{-}CO{-}CH}\\ \mathrm{Ph{\cdot}CH{\cdot}CHPh{\cdot}C{\cdot}CH_3}\end{matrix} + \mathrm{H_2O}.$$

Goldschmiedt and Krczmar (*ibid.*, p. 749) obtained the homologues of styryl benzyl ketone and 2 : 3 : 6-triphenyltetrahydro-4-pyrone from *p*-tolualdehyde, whilst anisaldehyde and piperonal gave the corresponding styryl ketones only. They state that the condensation of benzyl methyl ketone with salicylaldehyde, 2-methoxybenzaldehyde, cinnamaldehyde, and cuminaldehyde was attempted, but only viscous oils or resinous masses were obtained.

The condensation of benzyl methyl ketone with salicylaldehyde has now been fully investigated, two types of condensing agent—amines and sodium hydroxide—being used.

(1) With piperidine or diethylamine, a substance, $C_{16}H_{14}O_2$, was obtained formed according to the equation:

$$\mathrm{CH_2Ph{\cdot}CO{\cdot}CH_3 + HO{\cdot}C_6H_4{\cdot}CHO = C_{16}H_{14}O_2 + H_2O}.$$

Since the compound is an unsaturated phenolic ketone, the only possible structural formulæ are $\mathrm{HO{\cdot}C_6H_4{\cdot}CH{:}CH{\cdot}CO{\cdot}CH_2Ph}$ (I) and $\mathrm{HO{\cdot}C_6H_4{\cdot}CH{:}CPh{\cdot}CO{\cdot}CH_3}$ (II). The compound is regarded as 2-*hydroxystyryl benzyl ketone* (I), since its methyl ether is not identical with the compound obtained by condensing 2-methoxybenzaldehyde with benzyl methyl ketone in presence of hydrogen chloride. The latter compound is almost certainly the methyl ether of (II), since condensation in presence of acid always takes place preferentially at a methylene group. The possibility of the two methoxy-compounds being *cis-trans*-isomerides has not been overlooked, but it is considered unlikely in view of other work carried out in these laboratories (compare McGookin and Heilbron, J., 1924, **125**, 2099; McGookin and Sinclair, J., 1925, **127**, 2539).

(2) In the condensation by means of aqueous-alcoholic alkali, remarkable results were obtained. Although many variations in the experimental conditions were tried, no trace of the normal product (I) was detected. Five compounds together with traces of others were isolated, but the investigation of these was hampered

by the difficulty of separating them, and more particularly by the small amounts of pure material eventually obtained, much resinous matter being present. Further, only small quantities of material could be condensed at a time, otherwise a more than proportional increase in the formation of resinous by-products occurred.

The five substances all gave analytical values agreeing with the formula $C_{41}H_{36}O_4$:

$$3C_9H_{10}O+2C_6H_4(OH)\cdot CHO=C_{41}H_{36}O_4+3H_2O.$$

Other pairs of aldehydes and ketones have been found to condense in the same ratio, but in the cases previously studied only 2 mols. of water were lost (compare Kostanecki and co-workers, *Ber.*, 1896, **29**, 1488, 1495, 1891, 2245, 2248).

The five isomerides are designated A, B, C, D, and E. Whereas the last is yellow and dissolves readily in cold aqueous alkali to a deep red solution, from which it is precipitated unchanged on acidification, the other four substances are colourless, insoluble in cold aqueous alkali, and show interesting relationships to one another as will be seen from the following: Treatment of A with concentrated alcoholic potassium hydroxide gives a pale yellow solution which slowly becomes brownish-red. Addition of water produces no precipitate, but on acidification a yellow solid separates which is readily soluble in aqueous alkali. Crystallisation of this solid from alcohol or benzene produces B. B also reacts with alcoholic potash to give a red solution, but is recovered unchanged on dilution and acidification. C can be converted into D under precisely the same conditions. D, on being boiled in alcoholic solution with a few drops of concentrated hydrochloric acid for ½ hour, is converted into B. The series of changes is shown in the diagram:

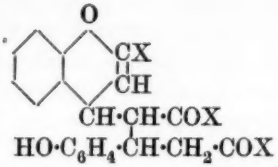
From these intimate relationships it follows that these substances must be very similar in structure. Probably they are stereoisomerides, similar cases having been noted by Kostanecki (*loc. cit.*) and Conant and Cutter (*J. Amer. Chem. Soc.*, 1926, **48**, 1016). They are probably derived from the unisolated intermediate compound, αγε-triphenylacetyl-βδ-di-*o*-hydroxyphenylpentane,

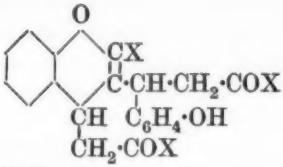
$$CH_2Ph\cdot CO\cdot CH[CH(C_6H_4\cdot OH)\cdot CH_2\cdot CO\cdot CH_2Ph]_2$$

(III), by loss of one molecule of water.

From the insolubility of the compounds in aqueous alkali, it may reasonably be inferred that at least one of the phenolic hydroxyl groups has been utilised in this secondary reaction, giving rise to pyran derivatives of the type (IV) or (V). These formulations are

supported to some extent by the fact that A readily yields a disemicarbazone.

(IV.) 

(V.) 

(X = CH_2Ph.)

Insolubility in alkali does not prove the absence of hydroxyl, for 2-hydroxybenzylidenediacetophenone is likewise insoluble (Cornelson and Kostanecki, *Ber.*, 1896, **29**, 240; Feuerstein and Kostanecki, *ibid.*, 1898, **31**, 710).

On methylation, A, B, and D give rise to dimethyl ethers, those of the former two, m. p. 135°, being identical. The dimethyl derivative of D melts at 138°, and at an intermediate temperature when mixed with the ether of A or B. This does not necessarily imply that they are identical, especially in view of the fact that repeated crystallisation of the lower-melting compound failed to alter the melting point. These ethers are not direct derivatives of (III), formed by the opening of the pyran ring in presence of alkali, but apparently correspond to enolic forms of (IV) or (V).

In E, which differs entirely from the other products, it is suggested that both phenolic hydroxyl groups are present. Owing to the difficulty of isolating this substance in appreciable quantity, experimental data in favour of any special structure could not be obtained.

Experimental.

2-Hydroxystyryl Benzyl Ketone.—A solution of benzyl methyl ketone (26·8 g.) and salicylaldehyde (24·4 g.) in absolute alcohol (40 c.c.) became orange-red on addition of piperidine (20 drops). A week later, more of the base (15 drops) was added to the syrupy liquid, from which, after a few days, bulky clusters of yellow needles slowly separated; these were periodically filtered off. The last crops contained an impurity, which coloured the solid pink and could not be removed by crystallisation or by treatment with charcoal. The residue was a dark red, viscous syrup. The product was twice crystallised from alcohol, giving clusters of long, colourless, silky needles (yield, 23 g.), m. p. 181°, which were insoluble in water but formed an orange solution in dilute aqueous sodium hydroxide. Exposed to light, the crystals rapidly became olive-green on the surface (Found: C, 80·5; H, 5·8. $C_{16}H_{14}O_2$ requires C, 80·7; H, 5·9%). The same compound was obtained when diethylamine was used instead of piperidine, but the yield was less satisfactory.

The *semicarbazone*, obtained in the usual manner, formed clusters

of short, colourless needles, m. p. 205—206° (Found: N, 14·2. $C_{17}H_{17}O_2N_3$ requires N, 14·2%). The *carbomethoxy*-derivative separated from alcohol in colourless needles, m. p. 64—65°.

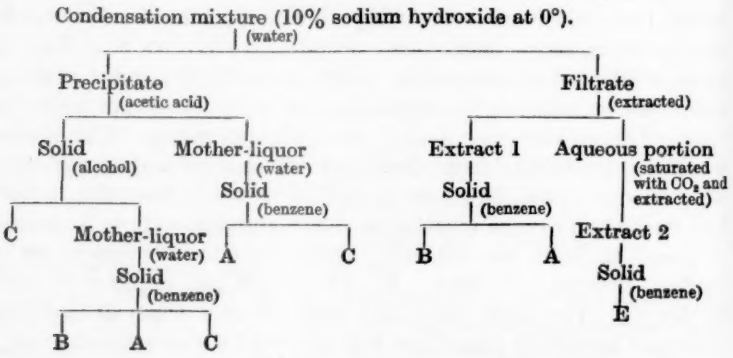
2-Methoxystyryl Benzyl Ketone.—2-Hydroxystyryl benzyl ketone was treated alternately with small quantities of methyl sulphate and 8% potassium hydroxide solution, at 30—40°, and continuously shaken, until addition of the alkali failed to produce a yellow colour. The separated solid crystallised from aqueous alcohol in long, lustrous, faintly yellow needles, m. p. 79° (Found: C, 80·4; H, 6·4. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4%).

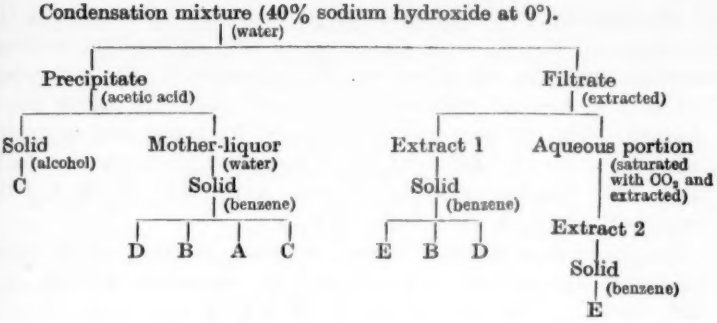
α-Phenyl-2-Methoxystyryl Methyl Ketone.

$$OMe{\cdot}C_6H_4{\cdot}CH{:}CPh{\cdot}CO{\cdot}CH_3.$$

—A solution of 2-methoxybenzaldehyde (5 g.) and benzyl methyl ketone (5 g.) in absolute alcohol (40 c.c.) was cooled in ice-water and saturated with a slow stream of dry hydrogen chloride. After several hours, the reddish-brown liquid was poured into water (300 c.c.) and rendered faintly alkaline. The precipitated semi-solid, yellow mass was taken up in ether, and after drying, the bulk of the solvent was removed. The crystalline deposit was twice crystallised from alcohol, being obtained in colourless rhombs which, when viewed in bulk, showed a faint pink colour; m. p. 145° (yield, 3·5 g.) (Found: C, 81·1; H, 6·1. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4%).

Condensation of Benzyl Methyl Ketone and Salicylaldehyde by Means of Sodium Hydroxide.—The condensation was usually carried out with equal tenth-molecular quantities of the reactants. Various temperatures were employed and the concentration of the alkali (of which at least 2 mols. were always used) was varied from 2% to 40%. The type of condensation most fully studied was as follows: A solution of benzyl methyl ketone (13·4 g.) and salicylaldehyde (12·2 g.) in alcohol (50 c.c.) was cooled in ice-water, and 10% sodium hydroxide solution (80 c.c.) slowly added. The pale red





solution became ruby-red after remaining for 3 days in the ice chest. The method of working is best followed from the accompanying charts, of which the following is a brief description. The condensation mixture was poured into water (1000 c.c.) and kept until the colloidal precipitate had coagulated. The resulting yellow solid was crystallised from glacial acetic acid, and the separated crystals (product C) were recrystallised from alcohol. The acetic acid mother-liquor was diluted with water, and the precipitate fractionally crystallised from benzene. The original aqueous filtrate was extracted with ether, saturated with carbon dioxide, and again extracted. After being washed and dried, the ethereal solutions were concentrated and the solid separating in each case was fractionally crystallised from benzene.

Condensation by means of hot 40% sodium hydroxide solution yielded a product which gave no precipitate on dilution and contained no substance A. Condensation by 2% sodium hydroxide at room temperature gave none of the products recognised above, but in this case no material has yet been obtained in sufficient quantity for investigation.

Substance A, which was the main product of most of the condensations studied, separated from benzene, carbon disulphide, or carbon tetrachloride as a white, micro-crystalline powder, m. p. 185° (decomp.). It is insoluble in water or cold aqueous alkali, moderately easily soluble in benzene, and readily soluble in alcohol. It does not noticeably react with bromine (Found: C, 83·4; H, 6·4. $C_{41}H_{36}O_4$ requires C, 83·1; H, 6·1%).

The *disemicarbazone*, prepared by the usual method, separated from alcohol in colourless plates, softening with decomposition at 230°. Analysis showed the compound to be impure, but recrystallisation was not attempted owing to lack of material (Found: N, 10·4. The mono- and the di-semicarbazone require N, 6·5 and 11·9% respectively).

The *dimethyl ether* was obtained by keeping a solution of A (1 g.) in acetone (50 c.c.) with an excess of 40% potassium hydroxide solution until the red colour was fully developed and then treating it slowly at 40—50° with methyl sulphate until the colour was discharged. The product was precipitated by water and crystallised twice from alcohol, from which it separated in colourless needles, m. p. 135° [Found: C, 83·4; H, 6·6; OMe, 8·9. $C_{41}H_{34}O_2(OMe)_2$ requires C, 83·2; H, 6·5; OMe, 10·0%].

Substance B crystallised from benzene in rosettes of minute, colourless needles and from alcohol in colourless rhombs, m. p. 228° (decomp.) (Found: C, 83·3; H, 6·1%).

Conversion of A into B.—A solution of A (1 g.) in alcohol (40 c.c.) was treated with 60% potassium hydroxide solution (5 c.c.) and kept at room temperature for 3 hours, its colour changing from yellow to red. The diluted solution was acidified, and the precipitated solid crystallised from alcohol. Its identity with B was proved by a mixed melting-point determination.

Substance B, treated in the same way, was recovered unchanged. Its alkaline solution, on methylation, gave a product identical with that obtained from A.

Substance C crystallised from benzene or alcohol in colourless needles, m. p. 186° (Found: C, 83·1; H, 6·2%). The m. p. of a mixture with A showed a considerable depression.

Substance D separated from benzene as a white, micro-crystalline powder, m. p. 209° (decomp.), containing 1 mol. of benzene of crystallisation. It was always found accompanying A, and its resemblance to the latter rendered separation of the two difficult (Found: C, 84·2; H, 6·3. $C_{41}H_{36}O_4,C_6H_6$ requires C, 84·2; H, 6·2%). Its dimethyl ether separated from alcohol in the same crystalline form as that from A and B, but melted at 138° (Found: C, 82·7; H, 6·6; OMe, 9·1%).

Conversion of C into D.—This was carried out in the same manner as that of A into B, except that the product was crystallised from benzene.

Conversion of D into B.—An alcoholic solution of D was treated with a few drops of concentrated hydrochloric acid, and the whole gently boiled under reflux for ½ hour; after cooling, the product was diluted with water. The dried solid was crystallised first from benzene and then from alcohol. It was identified with B both by its crystalline form and by the m. p. of a mixture of the two. Under the same conditions, A, B and C remained unchanged.

Substance E separated from benzene as a canary-yellow, micro-crystalline powder, m. p. 239° (decomp.). It was insoluble in water, but dissolved readily in cold aqueous sodium hydroxide, to a deep

red solution. In the condensation mixture, it was always accompanied by other yellow compounds, but the amounts of these were too minute for investigation (Found : C, 83·1; H, 5·9%).

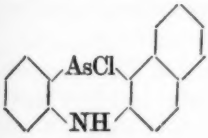
In conclusion, I wish to express my gratitude to the Advisory Council of the Department of Scientific and Industrial Research for a maintenance grant, and to the Lancashire Education Committee for the renewal of a scholarship during the tenure of which this research was carried out. My thanks are also due to Professor I. M. Heilbron, D.S.O., D.Sc., whose advice and encouragement have been of great value, and to Mr. E. Formby, M.Sc., for much assistance in the preliminary work.

THE UNIVERSITY, LIVERPOOL. [*Received, May 29th*, 1926.]

CCXCVI.—10-*Chloro*-5 : 10-*dihydrophenarsazine and its Derivatives. Part III. Homologues and Amino-, Chloro-, and Cacodyl Derivatives.*

BY HAROLD BURTON and CHARLES STANLEY GIBSON.

THE reaction between arsenious chloride and diphenylamine and its homologues has already been shown (Burton and Gibson, this vol., pp. 455, 466) to be of general applicability. The condensations of arsenious chloride with phenyl-β-naphthylamine, with *p*-tolyl-α-naphthylamine and with p-tolyl-β-naphthylamine, yielding 12-*chloro*-7 : 12-*dihydrobenzophenarsazine* (I), 7-*chloro*-9-*methyl*-7 : 12-*dihydrobenzophenarsazine* (II), and 12-*chloro*-10-*methyl*-7 : 12-*dihydrobenzophenarsazine* (III), respectively, are further instances of the general



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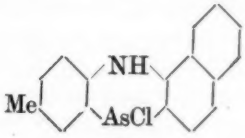

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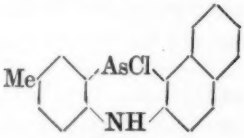
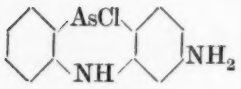


(III.)

reaction and are described in the present communication. The compound obtained by condensing arsenious chloride with phenyl-α-naphthylamine, namely, 7-chloro-7 : 12-dihydrobenzophenarsazine, is isomeric with (I) and has already been described by Lewis and Hamilton (*J. Amer. Chem. Soc.*, 1921, **43**, 2218; compare Burton and Gibson, this vol., p. 470).

Wieland and Rheinheimer (*Annalen*, 1921, **423**, 1) showed that *m*-aminodiphenylamine condenses readily with arsenious chloride and they assign formula (IV), 10-chloro-3-amino-5 : 10-dihydro-

phenarsazine, to the product. There is the possibility of the formation of an isomeric compound, (V), 10-chloro-1-amino-5 : 10-dihydrophenarsazine, but like the previous workers we have been unable to isolate a second product from the reaction. (This and the other amino-derivatives are most conveniently isolated in the form of the hydrochlorides.) The probable correctness of formula (IV) follows from the work of Roberts and Turner (J., 1925, **127**, 2005), who have shown that 3 : 10-dichlorophenoxarsine (VI) is exclusively formed when *m*-chlorodiphenyl ether is condensed with arsenious chloride.



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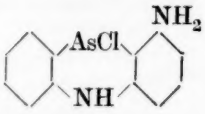

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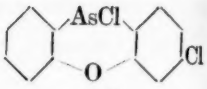
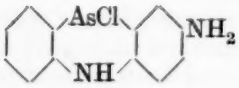
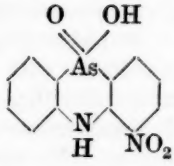


(VI.)

A second amino-derivative was obtained by Wieland and Rheinheimer (*loc. cit.*) by reducing the mononitrophenarsazinic acid, obtained from 10-chloro-5 : 10-dihydrophenarsazine by nitration and subsequent oxidation, first to the amino-acid and then to the chloroaminodihydrophenarsazine. To this compound they assigned the formula (VII), 10-chloro-2-amino-5 : 10-dihydrophenarsazine.

(VII.)




(VIII.)

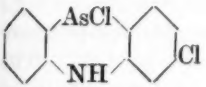
We have obtained the same compound by condensing arsenious chloride with *p*-aminodiphenylamine and thereby proved the correctness of the constitution assigned to it by Wieland and Rheinheimer.

By the nitration of phenarsazinic acid, Wieland and Rheinheimer obtained a nitrophenarsazinic acid to which they ascribed constitution (VIII), 4-nitrophenarsazinic acid. They also obtained the corresponding amino-acid. We have carried the reduction one stage further and obtained the corresponding 10-chloro-compound, the third of this series. This compound, which is different from either (IV) or (VII), cannot be 10-chloro-4-amino-5 : 10-dihydrophenarsazine corresponding to the constitution of Wieland and Rheinheimer's nitrophenarsazinic acid. On diazotisation, the amino-acid from which it is prepared does not yield a triazole derivative but a product which couples normally with β-naphthol. Consequently, the chloro-compound prepared from the nitration product of phenarsazinic acid must be 10-chloro-1-amino-5 : 10-dihydrophenarsazine

(V) referred to above, and the product of the nitration of phenarsazinic acid obtained by us must be 1-nitrophenarsazinic acid.

Arsenious chloride readily reacts with both *m*- and *p*-chlorodiphenylamines and the condensation products, 3 : 10-*dichloro*-5 : 10-*dihydrophenarsazine* (IX) and 2 : 10-*dichloro*-5 : 10-*dihydrophenarsazine* (X) respectively, have very similar properties to those of the parent substances. In a similar manner, 2 : 8 : 10-*trichloro*-5 : 10-*dihydrophenarsazine* (XI) has been prepared by condensing arsenious chloride with the now completely identified *pp'*-dichlorodiphenylamine.*

Hypophosphorous acid reduces the more soluble of these derivatives, either in the form of the chloro-compounds or as the phenarsazinic acids, in aqueous acetone–alcohol or acetic acid solution to the corresponding cacodyl compounds. Of these, only 10 : 10'-



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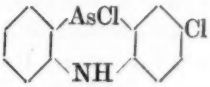
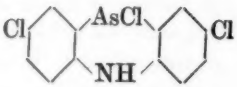


(X.)



(XI.)

bis-5 : 10-*dihydrophenarsazine* and the corresponding *diacetyl* derivative are now described. These two sparingly soluble compounds are moderately stable and do not change during isolation under ordinary conditions. On the other hand, the cacodyl compounds obtained in a similar manner from 10-chloro-2-methyl-5 : 10-dihydrophenarsazine and 3-aminophenarsazinic acid are too unstable to be isolated easily in a pure condition.

10 : 10'-Bis-5 : 10-dihydrophenarsazine is converted by bromine in carbon tetrachloride solution into 10-bromo-5 : 10-dihydrophenarsazine and, when suspended in boiling xylene with free access of air, it is oxidised in a short time to the colourless phenarsazinic acid.

Experimental.

12-*Chloro*-7 : 12-*dihydrophenarsazine* (I) was prepared by boiling for 8 hours a mixture of phenyl-β-naphthylamine (10·9 g.), arsenious chloride (10 g.) and *o*-dichlorobenzene (30 c.c.). The crude compound (14·8 g.) was recrystallised from *s*-tetrachloroethane and

* The following compounds do not react directly with arsenious chloride to give dihydrophenarsazine derivatives: *o*-aminodiphenylamine, *pp'*-diaminodiphenylamine, *o*-, *m*-, and *p*-nitrodiphenylamines, *oo'pp'*-tetrachlorodiphenylamine. These negative results taken in conjunction with the positive results we have obtained indicate that arsenious chloride will condense with substituted diphenylamines as with diphenylamine, only when all the ortho-positions with respect to the nitrogen atom are free and when no nitro-substituting group is present. This does not hold, however, in the case of phenylene-substituting groups (compare this vol., p. 455).

obtained in yellow needles, m. p. 249—250° (Found: As, 22·6. $C_{16}H_{11}NClAs$ requires As, 22·9%).

7-*Chloro*-9-*methyl*-7 : 12-*dihydrobenzophenarsazine* (II) was prepared in a similar manner from *p*-tolyl-α-naphthylamine. Recrystallised from toluene, it was obtained in deep yellow needles, m. p. 252—255° (decomp.) (Found: As, 21·8. $C_{17}H_{13}NClAs$ requires As, 21·95%).

12-*Chloro*-10-*methyl*-7 : 12-*dihydrobenzophenarsazine* (III) was prepared similarly from *p*-tolyl-β-naphthylamine. The substance was obtained in yellow needles, m. p. 266—267° (decomp.), by recrystallisation from *s*-tetrachloroethane (Found: As, 21·8. $C_{17}H_{13}NClAs$ requires As, 21·95%).

On repeating the preparation of the hydrochloride of 10-chloro-3-amino-5 : 10-dihydrophenarsazine (IV) the product was found to be homogeneous. A mixture of *m*-aminodiphenylamine * (5 g.) and arsenious chloride (8 g.) was heated for 5 hours, the temperature of the oil-bath being gradually raised from 140° to 170°. The powdered residue was washed with dry ether and recrystallised from alcoholic hydrochloric acid. The compound (5 g.) crystallised in pale yellow prisms which do not melt below 300° (Found: Cl, 21·5. $C_{12}H_{11}N_2Cl_2As$ requires Cl, 21·6%).

The hydrochloride of 10-chloro-2-amino-5 : 10-dihydrophenarsazine (VII) was prepared in a similar manner from *p*-aminodiphenylamine. The product separated from alcoholic hydrochloric acid in greenish-yellow plates which do not melt below 300° (Found: Cl, 21·7. Calc. for $C_{12}H_{11}N_2Cl_2As$: Cl, 21·6%). This compound was identical with the compound prepared in a different manner by Wieland and Rheinheimer.

For the nitration of phenarsazinic acid a modification of Wieland and Rheinheimer's method was employed. A solution of phenarsazinic acid (20 g.) in hot glacial acetic acid (450 c.c.) was cooled rapidly to 15°, and fuming nitric acid (25 c.c.) added in small portions with thorough shaking, the temperature being maintained at 20—25°. After 1 hour, the yellow, crystalline solid was separated and washed with acetic acid and with ether. The crude nitrophenarsazinic acid (43 g. from two experiments) was dissolved in hot sodium hydroxide solution (500 c.c. containing 40 g. of NaOH), and the sodium salt allowed to crystallise. This salt was recrystallised from half the quantity of sodium hydroxide solution and, after separation, washed with dilute sodium hydroxide and finally

* The *m*-aminodiphenylamine was prepared by reducing *m*-nitrodiphenylamine with iron filings and acetic acid. It had m. p. 66—67° (Found: N, 15·4%). The m. p., 76—77°, given by Wieland and Rheinheimer is probably a misprint.

with water. The neutral sodium salt was converted into the *barium* salt in the usual manner and this was crystallised from water. It separated in silky, yellow needles containing seven molecules of water of crystallisation. The anhydrous barium salt had a beautiful bronze lustre (Found : H_2O, 14·4. $C_{24}H_{16}O_8N_4As_2Ba,7H_2O$ requires H_2O, 14·0%. Found in anhydrous salt : Ba, 17·7. $C_{24}H_{16}O_8N_4As_2Ba$ requires Ba, 17·7%). The barium salt, suspended in water, was treated with a slight excess of hydrochloric acid, and the nitrophenarsazinic acid (16·4 g.) filtered off, washed thoroughly with water, and dried. The acid, only slightly soluble in most solvents, can be conveniently crystallised from acetic acid, from which it separates in clusters of yellow needles which do not melt below 300°.

For the reduction to the amino-acid, a hot solution of the nitro-acid (9·5 g.) in dilute sodium hydroxide was added to a boiling suspension of ferrous hydroxide prepared by adding an excess of 25% sodium hydroxide solution to a hot solution of ferrous sulphate (50 g. in 150 c.c. of water). The mixture was well stirred for 10 minutes and, after filtration from ferric hydroxide, the amino-acid was isolated in quantitative yield by acidification of the filtrate. The solubility of the amino-acid in water is very small. The constitution of this amino-acid was proved by dissolving it in an excess of dilute hydrochloric acid and diazotising the solution in the cold with sodium nitrite; the resulting solution gave, with an alkaline solution of β-naphthol, a soluble red azo-compound.

The *dihydrochloride* was obtained by treating a suspension of the acid in hot alcohol with concentrated hydrochloric acid until crystalline matter began to separate. The dihydrochloride decomposed when heated to about 260° (Found : Cl, 21·5. $C_{12}H_{13}O_2N_2Cl_2As$ requires Cl, 21·5%).

The *hydrochloride* of 10-*chloro*-1-*amino*-5 : 10-*dihydrophenarsazine* (V) was obtained by dissolving the above amino-acid (8 g.) in a boiling mixture of alcohol (20 c.c.) and concentrated hydrochloric acid (10 c.c.) containing a trace of iodine. Sulphur dioxide was passed into the boiling solution until crystalline material separated. The crystals were filtered off and washed with alcoholic hydrochloric acid, absolute alcohol, and finally with ether. The hydrochloride of 10-chloro-1-amino-5 : 10-dihydrophenarsazine crystallises from alcoholic hydrochloric acid in yellow plates which begin to decompose at a high temperature (Found : Cl, 21·2. $C_{12}H_{11}N_2Cl_2As$ requires Cl, 21·6%).

m-Chlorodiphenylamine was made by the diazotisation treatment with cuprous chloride and subsequent hydrolysis of *N*-acetyl-*m*-aminodiphenylamine. It had b. p. 340°/766 mm. *p*-Chlorodi-

phenylamine was similarly prepared from *N*-acetyl-*p*-aminodiphenylamine. It was finally separated by steam distillation and had m. p. 66—67° (Ullmann, *Annalen*, 1910, **355**, 312, gives 74°).

The following is the method of preparation leading to the complete identification of pp'-*dichlorodiphenylamine*. A solution of *N*-formyl-*pp'*-diaminodiphenylamine (40 g.) in water (200 c.c.) and concentrated hydrochloric acid (100 c.c.) was cooled to 0° and diazotised with a solution of sodium nitrite (32 g.) in water. The diazo-solution was added gradually to a cold solution of cuprous chloride made from copper carbonate (24 g.), concentrated hydrochloric acid (240 c.c.), and excess of copper. After 5 hours, the crude formyl derivative was filtered off and extracted from inorganic matter with the minimum quantity of hot alcohol. Hydrolysis was effected by boiling the alcoholic solution for 1 hour with concentrated hydrochloric acid (100 c.c.). After removal of the alcohol, the dark-coloured residue was extracted with ether, the ethereal solution dried, and the ether distilled off. The crude dichloro-compound crystallised rapidly (31 g.) and was purified by extraction in the cold with ligroin (b. p. 40—60°). On concentrating this solution, *pp'*-dichlorodiphenylamine was obtained in almost colourless crystals, m. p. 71—72° (Found : Cl, 29·6. $C_{12}H_9NCl_2$ requires Cl, 29·8%).

3 : 10-*Dichloro*-5 : 10-*dihydrophenarsazine* (IX) was prepared by heating a mixture of *m*-chlorodiphenylamine (10·3 g.), arsenious chloride (10 g.), and *o*-dichlorobenzene (40 c.c.) under reflux for 7 hours. Hydrogen chloride was evolved steadily. On cooling, the crude chloro-compound separated in yellow needles (7·2 g.). 3 : 10-Dichloro-5 : 10-dihydrophenarsazine crystallised from benzene in yellow needles, m. p. 220—221° (decomp.) (Found : As, 23·9. $C_{12}H_8NCl_2As$ requires As, 24·0%).

2 : 10-*Dichloro*-5 : 10-*dihydrophenarsazine* (X) was prepared from *p*-chlorodiphenylamine in an exactly similar manner. The compound was recrystallised from glacial acetic acid and obtained in yellow needles, m. p. 230—231° (decomp.) (Found : As, 23·8. $C_{12}H_8NCl_2As$ requires As, 24·0%).

2 : 8 : 10-*Trichloro*-5 : 10-*dihydrophenarsazine* (XI) was prepared by boiling for 12 hours a mixture of *pp'*-dichlorodiphenylamine (11·9 g.), arsenious chloride (10 g.), and *o*-dichlorobenzene (20 c.c.). The product, which separated on cooling, crystallised from acetic acid in yellow needles, m. p. 273—274° (decomp.) (Found : As, 21·3; Cl, 30·1. $C_{12}H_7NCl_3As$ requires As, 21·6; Cl, 30·7%).

10 : 10'-*Bis*-5 : 10-*dihydrophenarsazine*, $[NH(C_6H_4)_2As]_2$, was prepared in two ways. (*a*) A hot solution of 10-chloro-5 : 10-dihydrophenarsazine (5·5 g.) in a mixture of alcohol (75 c.c.) and acetone

(100 c.c.) was treated with hypophosphorous acid (8 c.c., *d* 1·136) diluted with alcohol (15 c.c.). The solution became orange in colour, and, on cooling, orange-yellow needles of the cacodyl compound (2·7 g.) separated. (*b*) Phenarsazinic acid (5 g.) was dissolved in boiling acetic acid (120 c.c.) containing a trace of iodine. To the hot solution, hypophosphorous acid (quantity as above) was added. On cooling, crystals of the cacodyl compound (2·5 g.) separated identical in every respect with a sample prepared as above.

The cacodyl compound is very sparingly soluble in the usual organic solvents. It melts at 304—305° (decomp.) (Found: As, 30·8. $C_{24}H_{18}N_2As_2$ requires As, 31·0%). It is moderately stable under ordinary conditions, but when suspended in boiling acetone or xylene it is rapidly oxidised, producing the colourless phenarsazinic acid.

A suspension of the cacodyl compound (9·45 g.) in carbon tetrachloride was treated with a 10% solution of bromine in the same solvent. The colour of the bromine was discharged and crystals slowly separated which, after recrystallisation from acetic acid and then from toluene, were proved to be 10-bromo-5 : 10-dihydrophenarsazine by the m. p. and by the m. p. of a mixture with an authentic specimen.

10 : 10′-*Bis*-5-*acetyl*-5 : 10-*dihydrophenarsazine*, $[CH_3{\cdot}CO{\cdot}N(C_6H_4)_2As]_2$.—*N*-Acetylphenarsazinic acid (5 g.) was dissolved in boiling acetic acid (50 c.c.) containing a trace of iodine. To the hot solution hypophosphorous acid (quantity as above) was added. On cooling, the cacodyl compound separated in clusters of almost colourless needles, m. p. 293—294° after previous decomposition (Found: As, 26·3. $C_{28}H_{22}O_2N_2As_2$ requires As, 26·4%).

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CCXCVII.—*Derivatives of Naphthaquinolines and Naphthaisoquinolines.**

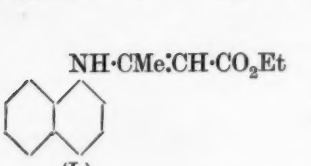
By CHARLES STANLEY GIBSON, KALVOI VENKATAKRISHNA HARIHARAN, KOTTIAZATH NARAYANA MENON, and JOHN LIONEL SIMONSEN.

IN continuation of the work (Gibson and Simonsen, J., 1915, **107**, 1148) which began with the stereochemical investigation of *dl*-tetra-

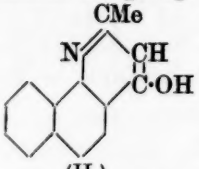
* The name naphthaquinoline is in established use and hence also the name naphtha*iso*quinoline has been adopted in the present communication. It

hydro-β-naphthaquinaldine [*dl*-3-methyl-1 : 2 : 3 : 4-tetrahydro-β-naphthaquinoline] it has been necessary to study some derivatives of the naphthaquinolines in greater detail than was at first anticipated. Whilst the condensation of β-naphthylamine and paraldehyde (Doebner and von Miller, *Ber.*, 1884, **17**, 1711) offers no difficulties, we have not been able to isolate the α-naphthaquinaldine—2-methyl-α-naphthaquinoline—by condensing α-naphthylamine with paraldehyde as described by the above authors; in numerous experiments, apart from unchanged material, we obtained only amorphous, brown solids. It would appear, therefore, that these authors worked under conditions which we have been unable to reproduce.

In order to obtain *dl*-tetrahydro-α-naphthaquinaldine [*dl*-2-methyl-1 : 2 : 3 : 4-tetrahydro-α-naphthaquinoline] we studied the method first adopted by Knorr (*Ber.*, 1884, **17**, 543) and subsequently investigated in greater detail by Conrad and Limpach (*Ber.*, 1888, **21**, 531). The latter authors state that when α-naphthylamine and ethyl acetoacetate are heated together for a long period on the water-bath ethyl β-1-naphthylaminocrotonate (I) is produced. Under these conditions we were able to isolate only acetoaceto-α-naphthalide (V), even when a considerable excess of ethyl acetoacetate was employed. In the presence of a small quantity of diethylamine, however, α-naphthylamine and ethyl acetoacetate readily condensed to give the desired compound (I). This compound was not obtained crystalline, but when the oil was heated to 240° it was converted into 4-hydroxy-2-methyl-α-naphthaquinoline (II). By the action of phosphorus pentachloride



(I.)



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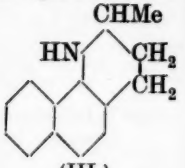


(III.)

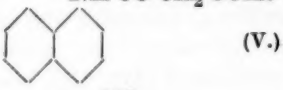
the corresponding 4-*chloro*-2-*methyl*-α-*naphthaquinoline* was easily obtained and this was reduced with sodium and ethyl alcohol to the desired compound, dl-2-*methyl*-1 : 2 : 3 : 4-*tetrahydro*-α-*naphthaquinoline* (III). This is the compound that should be obtained by the reduction of the base which Doebner and von Miller describe as having been prepared by the condensation of α-naphthylamine and paraldehyde. The compound is an oil which was readily characterised by the preparation of a number of derivatives.

should be pointed out, however, that the names benzoquinoline and benzo-*iso*quinoline would be preferable, as being in accordance with the system on which the majority of composite names of ring systems is devised; but no alteration is suggested, as the introduction of fresh synonyms is undesirable.

Under the conditions described by Knorr (*loc. cit.*) α-naphthylamine and ethyl acetoacetate alone yield only a small quantity of β-1-*naphthylaminocrotono*-1-*naphthylamide* (IV), the chief product of the reaction being a colourless, non-basic, high-melting substance *A* (p. 2254). Under the conditions described later, the amount of (IV) obtained is much more satisfactory. This compound exists in two interconvertible forms (see the experimental section), but it has not been determined whether this is a simple case of dimorphism or whether the two forms represent the possible *cis*- and *trans*-modifications.

The crotonyl derivative was readily converted into acetoaceto-α-naphthalide (V) by hydrolysis with dilute hydrochloric acid,

(IV.)



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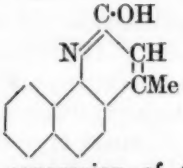
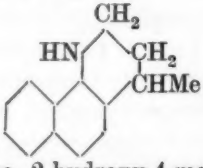


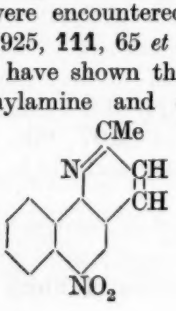
(VI.)



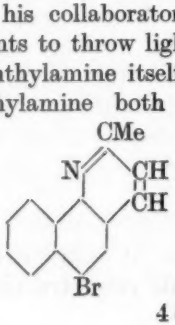
(VII.)

but the conversion of this product into 2-hydroxy-4-methyl-α-naphthaquinoline (VI) by means of concentrated hydrochloric acid presented great difficulties on account of hydrolysis and the production of α-naphthylamine. Sufficient of the hydroxy-base was obtained, however, for the preparation of the corresponding *chloro*-compound and the reduction of the latter to dl-4-*methyl*-1 : 2 : 3 : 4-*tetrahydro*-α-*naphthaquinoline* (VII). This base does not give a crystalline *benzoyl* derivative, but it is readily characterised by its crystalline *picrate*.

During the course of this work very marked differences in the behaviour of α- and β-naphthylamines towards paraldehyde and ethyl acetoacetate were repeatedly noticed, and similar difficulties in obtaining derivatives of α-naphthaquinoline from α-naphthylamine were encountered by John and his collaborators (*J. pr. Chem.*, 1925, **111**, 65 *et seq.*). Experiments to throw light on this problem have shown that, unlike α-naphthylamine itself, 4-nitro-α-naphthylamine and 4-bromo-α-naphthylamine both condense



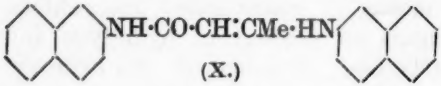
(VIII.)



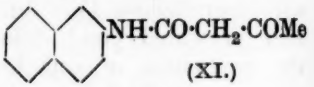
(IX.)

readily with paraldehyde, yielding 6-*nitro*-2-*methyl*-α-*naphthaquinoline* (VIII) and 6-*bromo*-2-*methyl*-α-*naphthaquinoline* (IX) respectively. Mr. Unni Nair and one of us (J. L. S.) have also recently found that 4-aminoacenaphthene condenses readily with paraldehyde, and thus we have definite evidence that substitution in the 4-position in α-naphthylamine seems to be a determining factor in making α-naphthylamine behave more nearly like β-naphthylamine.

By condensing β-naphthylamine and ethyl acetoacetate under the conditions described later (p. 2255; compare Knorr, *loc. cit.*, and Conrad and Limpach, *loc. cit.*), β-2-*naphthylaminocrotono*-2-*naphthylamide* (X) was readily obtained. From this compound, by hydrolysis with dilute hydrochloric acid, *acetoaceto*-β-*naphthalide* (XI) was prepared, and this, when heated with concentrated hydrochloric acid, was converted into 3-*hydroxy*-1-*methyl*-β-*naphthaquinoline* (XII). By reactions which have already been indicated, the corresponding 3-*chloro*-1-*methyl*-β-*naphthaquinoline* and dl-1-*methyl*-1 : 2 : 3 : 4-*tetrahydro*-β-*naphthaquinoline* (XIII) were obtained. This externally compensated base, like the analogous one prepared from α-naphthylamine, is a viscous oil which crystallises in liquid air. Its *benzoyl* derivative could not be obtained crystalline, but the crystalline *picrate* serves for its easy characterisation.

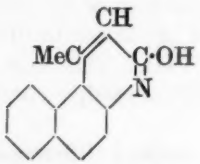


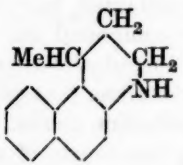
(X.)



(XI.)

(XII.)





(XIII.)

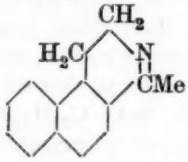
Under suitable conditions, the reaction between β-naphthylamine and ethyl acetoacetate goes differently from that described above and a colourless, non-basic, high-melting substance, *B* (p. 2257), is formed. This is isomeric with substance *A* (p. 2254), with which it has been carefully compared. The substances *A* and *B* are undoubtedly the ureas, $CO(NH{\cdot}C_{10}H_7)_2$, of α- and β-naphthylamine respectively and their formation is explicable by the mechanism suggested by Hurst and Thorpe (J., 1915, **107**, 934; compare Ewins and King, J., 1913, **103**, 104; Young and Clark, J., 1897, **71**, 1200).

The possible occurrence in nature of naphtha*iso*quinoline derivatives made it desirable to attempt the preparation of compounds having this ring structure, no representatives of which seem to

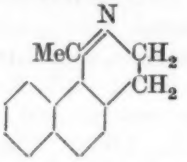
have been described. Our work is based on that of Kaufmann and Radosević (*Ber.*, 1916, **49**, 675), who treated the oximes of substituted γ-ketobutylbenzenes with phosphorus pentoxide and obtained methyldihydro*iso*quinoline derivatives.

The considerable quantities of α- and β-naphthaldehydes required were conveniently prepared by Sonn and Müller's method (*Ber.*, 1919, **52**, 1927). α- and β-Naphthaldehydes condensed readily with acetone to give 1- and 2-*γ-ketobutenylnaphthalenes*, $C_{10}H_7$·CH:CH·COMe, respectively, from which the corresponding *γ-ketobutylnaphthalenes*, $C_{10}H_7$·CH_2·CH_2·COMe, were obtained by catalytic reduction. These were converted into the corresponding *oximes*, and, although the preparation from these of the dihydrobases was attended by the formation of much resinous by-product, sufficient 4-*methyl*-1 : 2-*dihydro*-β-*naphtha*isoquinoline (XIV) (from α-naphthaldehyde) and 1-*methyl*-3 : 4-*dihydro*-α-*naphtha*isoquinoline (XV) (from β-naphthaldehyde) were obtained in the crystalline condition for identification. The following scheme represents the formation of these compounds.

$$C_{10}H_7\cdot CH_2\cdot CH_2\cdot CMe{:}NOH \longrightarrow [C_{10}H_7\cdot CH_2\cdot CH_2\cdot N{:}CMe\cdot OH] \longrightarrow$$



(XIV.)



(XV.)

The stereochemical investigation of the externally compensated bases now described is in progress.

Experimental.

Condensation of α-Naphthylamine and Ethyl Acetoacetate.—A mixture of ethyl acetoacetate (13 g.) and α-naphthylamine (14·3 g.) containing 2 drops of 33% diethylamine solution became cloudy in a few hours and the calculated quantity of water had separated in 3 days. The thick, red oil was extracted with ether, the solution dried, and the ether distilled. The residual oil, when heated at 240°, was converted into a crystalline solid, which was ground with alcohol and crystallised from amyl alcohol or nitrobenzene. As stated by Conrad and Limpach, the 4-hydroxy-2-methyl-α-naphthaquinoline (II) did not melt below 300° (Found : N, 7·1. Calc. : N, 6·7%).

4-*Chloro*-2-*methyl*-α-*naphthaquinoline.*—A mixture of 4-hydroxy-2-methyl-α-naphthaquinoline (10 g.), tetrachloroethane (20 c.c.) and phosphorus pentachloride (10 g.) was heated at 130—140° for 2 hours and finally at 160—170° for 1 hour; evolution of

hydrogen chloride had then ceased. The clear, deep brown solution, which deposited crystals on cooling, was poured on to ice; the greater part of the chloro-derivative separated in the form of the sparingly soluble hydrochloride. A solution of this in hot water was filtered from a little tar and basified, the chloro-derivative separating as a colourless, crystalline solid. A further quantity was obtained from the tetrachloroethane solution by removal of the solvent with steam and basification of the filtered acid solution. 4-*Chloro*-2-*methyl*-α-*naphthaquinoline* crystallised from alcohol, in which it was somewhat sparingly soluble, in long needles, m. p. 92—93° (Found : N, 6·6. $C_{14}H_{10}NCl$ requires N, 6·2%). The *picrate*, prepared from equivalent quantities of the base and picric acid in alcoholic solution, separated in yellow prisms, m. p. 196—197°, which could not be recrystallised owing to their sparing solubility.

dl-2-*Methyl*-1 : 2 : 3 : 4-*tetrahydro*-α-*naphthaquinoline* (III).—To a solution of 4-chloro-2-methyl-α-naphthaquinoline (20 g.) in boiling alcohol (900 c.c.), sodium (60 g.) was added as rapidly as possible. When all the sodium had dissolved, the alcohol was removed in steam, the residual oil extracted with ether, and the ether dried and evaporated. On distillation under diminished pressure, the base was obtained as a pale yellow, somewhat mobile, uncrystallisable oil, b. p. 202—203°/20 mm. In solution it showed a marked blue fluorescence (Found : C, 85·0; H, 8·0. $C_{14}H_{15}N$ requires C, 85·3; H, 7·6%). The *benzoyl* derivative crystallised from methyl alcohol, in which it was readily soluble, in clusters of colourless needles, m. p. 102—103° (Found : N, 4·7. $C_{21}H_{19}ON$ requires N, 4·6%). The *hydrochloride* crystallised from hot dilute hydrochloric acid, in which it was somewhat sparingly soluble, in glistening prisms, decomp. 252—253° (Found : Cl, 15·2. $C_{14}H_{15}N,HCl$ requires Cl, 15·2%). The *sulphate* crystallised from dilute sulphuric acid in iridescent prisms, decomp. 211—212° (Found : S, 10·6. $C_{14}H_{15}N,H_2SO_4$ requires S, 10·9%). The *chloroplatinate* was a very sparingly soluble, brown powder, decomp. 207—208°. The *picrate* crystallised from dilute alcohol in fine, yellow needles, m. p. 88—89°. These evidently contained solvent of crystallisation, for, after being dried in a vacuum over calcium chloride prior to analysis, they melted at 153—154° and decomposed at a slightly higher temperature (Found : N, 13·4. $C_{20}H_{18}O_7N_4$ requires N, 13·1%).

β-1-*Naphthylaminocrotono*-1-*naphthylamide* (IV).—A mixture of α-naphthylamine (2 mols.) and ethyl acetoacetate (1 mol.) was heated on the water-bath for 24 hours and then at 150—170° for 4 hours. The semi-solid red condensation product was extracted

with boiling 88% alcohol; a considerable quantity of the crystalline solid *A* remained undissolved. The filtrate, when kept in the ice chest, slowly deposited β-1-*naphthylaminocrotono*-1-*naphthylamide*, and a further quantity was obtained by removing the alcohol and grinding the residue with benzene or light petroleum. The substance usually separated from the alcoholic solution as a fine, crystalline powder, m. p. 135—145°, but occasionally it was deposited in well-formed needles, m. p. 145—147°. It was apparently dimorphous and the crystalline form and m. p. varied according to the solvent used for crystallisation. When crystallised from absolute alcohol, the compound separated in well-formed, prismatic needles, m. p. 167—168°, and this m. p. was unaltered by recrystallisation from this solvent. From benzene, the compound was deposited in fine, silky needles which softened at 135° and melted at 144—145°. Crystallisation of the substance of higher m. p. from benzene yielded the form, m. p. 144—145°, which could be reconverted into the form of higher m. p. by crystallisation from alcohol. The lower-melting form was also converted into the higher-melting form by heating it above its melting point, since, after solidification in the m. p. tube, the m. p. was 167—168°. Both forms had the same composition [Found: (1) C, 81·8; H, 5·6. (2) C, 81·3; H, 6·0. $C_{24}H_{20}ON_2$ requires C, 81·8; H, 5·7%].

Acetoaceto-α-naphthalide (V) was obtained in a quantitative yield when the preceding compound was digested on the water-bath with 4% hydrochloric acid for ½ hour. It crystallised from benzene in needles, m. p. 107° (Found: N, 6·2. $C_{14}H_{13}O_2N$ requires N, 6·2%).

The finely divided naphthalide, after remaining in contact with concentrated hydrochloric acid for some weeks, was converted into 2-hydroxy-4-methyl-α-naphthaquinoline (VI), which crystallised from alcohol in needles having the m. p. recorded by Knorr.

2-*Chloro*-4-*methyl*-α-*naphthaquinoline* was obtained when the hydroxy-quinoline was heated at 130—140° with the required amount of phosphorus pentachloride for 2 hours. The product, after treatment with dilute alkali, was dissolved in cold concentrated hydrochloric acid, filtered from a little resin, and precipitated by addition of water. It crystallised from alcohol in prisms, m. p. 134—135° (Found: Cl, 15·3. $C_{14}H_{10}NCl$ requires Cl, 15·6%).

dl-4-*Methyl*-1 : 2 : 3 : 4-*tetrahydro*-α-*naphthaquinoline* (VII), prepared by reducing the preceding chloro-compound under the conditions employed in the reduction of 4-chloro-2-methyl-α-naphthaquinoline (see p. 2252), was obtained as a viscous, pale yellow, uncrystallisable oil, b. p. 186—188°/10 mm. (Found: C, 85·0; H, 7·8. $C_{14}H_{15}N$ requires C, 85·3; H, 7·6%).

It showed a bluish-green fluorescence in benzene or alcohol and the solution darkened rapidly on exposure to the air. The sulphate and hydrochloride were somewhat readily soluble in water, the hydrobromide more sparingly soluble. The *picrate* crystallised from much alcohol in pale yellow prisms, decomp. 205—206° (Found : N, 13·6. $C_{20}H_{18}O_7N_4$ requires N, 13·1%).

The substance *A* produced in the condensation of α-naphthylamine and ethyl acetoacetate (see p. 2253) became the main product if the preliminary heating on the water-bath was omitted. It was very sparingly soluble in all the ordinary solvents and had no basic properties. It crystallised from much acetic acid or from nitrobenzene in fine needles, decomp. 280°. When distilled with zinc dust, or heated with hydrochloric acid or alcoholic potassium hydroxide in a sealed tube at 150°, it gave α-naphthylamine only, and oxidations with potassium permanganate in acid solution produced phthalic acid (Found : C, 81·05, 80·9; H, 5·1, 5·15; N, 9·0, 8·9. Calc. for $C_{21}H_{16}ON_2$: C, 80·8; H, 5·2; N, 9·0%). It was proved to be the urea of α-naphthylamine by comparison with an authentic specimen.

Condensation of 4-Nitro-α-naphthylamine and Paraldehyde.—A mixture of 4-nitro-α-naphthylamine (20 g.), concentrated hydrochloric acid (40 g.), and paraldehyde (30 g.) was heated at 110—115° for 4 hours with constant agitation. The cooled reaction mixture was poured into water, the solid collected and repeatedly triturated with concentrated hydrochloric acid. The filtered solution was diluted with water until no further precipitate formed, and after remaining over-night the yellow solid, which was not investigated, was removed and the acid solution basified. The dark brown solid thus precipitated was dried (5 g.) and repeatedly extracted with boiling light petroleum (b. p. 60—80°), which left undissolved a considerable quantity of carbonaceous matter. The petroleum solution slowly deposited a greenish-yellow, crystalline solid which, after recrystallisation from alcohol with the aid of animal charcoal, was obtained in soft, yellow needles, m. p. 141—142° (Found : N, 11·8. $C_{14}H_{10}O_2N_2$ requires N, 11·8%).

6-Nitro-2-methyl-α-naphthaquinoline (VIII) is very soluble in all the ordinary organic solvents except alcohol and light petroleum. The sulphate and hydrochloride are readily soluble in water; the nitrate, which crystallises in needles, is less soluble. The *chloroplatinate* is very sparingly soluble in water, crystallising in glistening, golden prisms, decomp. 229—230° [Found : Pt, 22·5. $(C_{14}H_{10}O_2N_2)_2,H_2PtCl_6$ requires Pt, 22·0%].

Condensation of 4-Bromo-α-naphthylamine and Paraldehyde.—A mixture of 4-bromo-α-naphthylamine hydrochloride (10 g.), par-

aldehyde (15 g.), and hydrochloric acid (20 g.) was heated at 110° for 4 hours. The cooled reaction mixture was mixed with alkali, and the deep brown solid which separated was collected. This was dissolved in hydrochloric acid, the non-basic impurities were separated by filtration, the solution was boiled with animal charcoal, and the mixture of bases reprecipitated with alkali. The crude bases were collected, dissolved in dilute sulphuric acid, treated with an excess of sodium nitrite solution to remove any primary and secondary bases, and the filtered solution basified. The crystalline base (2 g.) was purified by solution in light petroleum and finally recrystallised from methyl alcohol, from which it separated in colourless, felted needles, m. p. 99—100° (Found: N, 5·1; Br, 29·4. $C_{14}H_{10}NBr$ requires N, 5·1; Br, 29·4%).

6-Bromo-2-methyl-α-naphthaquinoline (IX) is readily soluble in benzene, ethyl acetate, or light petroleum, and more sparingly soluble in ethyl or methyl alcohol. It is insoluble in water. The hydrochloride separated from concentrated hydrochloric acid in needles which were readily soluble in water. The hydrobromide was somewhat more sparingly soluble and crystallised in prismatic needles. The *chloroplatinate* was a microcrystalline, brown powder, very sparingly soluble in water or dilute hydrochloric acid; it decomposed at 238° [Found: Pt, 20·2. $(C_{14}H_{10}NBr)_2,H_2PtCl_6$ requires Pt, 20·4%]. The *picrate* separated from alcohol, in which it was very sparingly soluble, in glistening, yellow prisms, m. p. 185—186°, and slowly decomposed above this temperature (Found: N, 11·6. $C_{20}H_{13}O_7N_4Br$ requires N, 11·2%).

Condensation of β-Naphthylamine and Ethyl Acetoacetate.—3-Hydroxy-1-methyl-β-naphthaquinoline (XII) was most conveniently prepared by the following modification of Knorr's method (*loc. cit.*). A mixture of β-naphthylamine (2 mols.) and ethyl acetoacetate (1 mol.) was heated on the water-bath for 12 hours and at 150—180° for 3 hours. The crystalline magma thus produced was cooled, crushed, and after removal of a little adherent oil, was well washed with hot alcohol. The crude β-2-naphthylaminocrotono-2-naphthylamide (X) was dissolved in much boiling xylene and filtered from a small quantity of sparingly soluble residue, *B* (see below) (yield 71%). The properties of the recrystallised substance agreed in all respects with Knorr's description. Acetoaceto-β-naphthalide (XI) was prepared from it by Knorr's method; the solution, however, was not boiled, the hydrolysis taking place readily on the water-bath. The naphthalide separated, on cooling, as a curious, gelatinous solid which could not be filtered and was therefore isolated by extraction with ethyl acetate, in which it was very readily soluble (yield 94%).

3-Hydroxy-1-methyl-β-naphthaquinoline was obtained when the naphthalide was heated on the water-bath with concentrated hydrochloric acid. If the solution was boiled as recommended by Knorr, a considerable quantity of β-naphthylamine was formed simultaneously.

When distilled with zinc dust, the hydroxy-compound gave a poor yield of 1-methyl-β-naphthaquinoline, m. p. 91—92°, the *picrate* of which, after crystallisation from much alcohol, melted at 230—231° with previous softening (Found : N, 12·5. $C_{20}H_{14}O_7N_4$ requires N, 13·3%).

3-*Chloro*-1-*methyl*-β-*naphthaquinoline*.—A mixture of 3-hydroxy-1-methyl-β-naphthaquinoline (5 g.), tetrachloroethane (10 c.c.), and phosphorus pentachloride (5·5 g.) was heated at 170—180° for 3 to 4 hours. The solvent and the phosphorus oxychloride were then removed under diminished pressure, and the residual solid, after trituration with dilute alkali, was crystallised from alcohol; the *chloro*-compound was thus obtained in colourless needles, m. p. 153—154° (yield 95%) (Found : Cl, 15·6. $C_{14}H_{10}NCl$ requires Cl, 15·6%).

dl-1-*Methyl*-1 : 2 : 3 : 4-*tetrahydro*-β-*naphthaquinoline* (XIII) was obtained when 3-chloro-1-methyl-β-naphthaquinoline was reduced under conditions similar to those employed for the preparation of *dl*-2-methyl-1 : 2 : 3 : 4-tetrahydro-α-naphthaquinoline (p. 2252). The greater part of the base distilled at 188—195°/10 mm., but was contaminated with a considerable quantity of resinous impurity which was only removed with difficulty by fractional distillation. The base was therefore converted into the *picrate*, which crystallised from alcohol in pale yellow needles; these decomposed at 162°, and at 167—168° when rapidly heated (Found : C, 56·2; H, 4·4; N, 13·1. $C_{20}H_{18}O_7N_4$ requires C, 56·3; H, 4·2; N, 13·1%). During the purification of the picrate a very small amount of a very sparingly soluble *picrate* was separated which crystallised from a large volume of alcohol in glistening, yellow leaflets, m. p. 201—202°. This picrate had the same composition as the picrate, m. p. 162° (Found : C, 56·1; H, 4·2%), but it was not obtained in sufficient quantity for investigation.

dl-1-*Methyl*-1 : 2 : 3 : 4-*tetrahydro*-β-*naphthaquinoline* regenerated from the picrate was a thick, yellow oil, b. p. 187—190°/10 mm., which darkened rapidly on exposure to air (Found : C, 84·8; H, 7·6. $C_{14}H_{15}N$ requires C, 85·3; H, 7·6%). It showed a blue fluorescence in benzene solution. It did not solidify in a freezing mixture, but at the temperature of liquid air it set to a crystalline mass of long needles which melted at room temperature. The hydrochloride was readily soluble in water; the sulphate, which crystallised in needles, was not so soluble.

The sparingly soluble substance, *B*, obtained during the condensation of β-naphthylamine and ethyl acetoacetate was formed in much larger quantity if the preliminary heating on the water-bath was omitted. This substance (compare substance *A*, p. 2254) was insoluble in all the ordinary organic solvents, but crystallised from nitrobenzene in large, colourless needles sintering at 288° and decomposing at 293—294° (Found: C, 80·8, 80·8; H, 5·1, 5·1; N, 8·9, 8·95%. Calc. for $C_{21}H_{16}ON_2$: C, 80·8; H, 5·2; N, 9·0%). It was shown to be the urea of β-naphthylamine by comparison with an authentic specimen.

1-*Methyl*-3 : 4-*dihydro*-α-*naphthaisoquinoline* (XV).—For the preparation of β-naphthaldehyde, a mixture of β-*naphthanilide* * (8 g.), tetrachloroethane (25 c.c.), and phosphorus pentachloride (7 g.) was heated at 140—150° until evolution of hydrogen chloride ceased (1 hour). The phosphorus oxychloride and a part of the solvent were removed under diminished pressure; on cooling, the iminochloride separated as a yellow, crystalline solid. This was redissolved in tetrachloroethane, and the solution gradually added to an ethereal solution of stannous chloride saturated with hydrogen chloride (ether, 250 c.c.; stannous chloride, 30 g.). A somewhat vigorous reaction took place and the stannichloride of the Schiff's base separated as a yellow, gelatinous solid. After some hours, the ether was decanted from the salt, dilute hydrochloric acid (50 c.c.) added, and the aldehyde distilled in steam (yield 80—90%).

2-γ-*Ketobutenylnaphthalene*.—A mixture of the aldehyde (1 part), acetone (6 parts), water (30 parts), and 20% sodium hydroxide solution (0·2 part) was agitated, and occasionally warmed on the water-bath, for 2 or 3 days. The aldehyde gradually liquefied and remained as a semi-solid oil until the condensation was nearly complete; the butenyl derivative then separated as a crystalline solid. When the reaction was complete, the solid was collected and dissolved in benzene, a small quantity of *di*-β-*naphthylvinyl ketone* (see below) remaining undissolved. The benzene solution was dried and evaporated.

2-γ-*Ketobutenylnaphthalene* separated from methyl alcohol in nodules of yellow needles, m. p. 102, after sintering at 95—96°. It was readily soluble in the ordinary organic solvents, but very sparingly soluble in water (Found: C, 85·5; H, 6·3. $C_{14}H_{12}O$ requires C, 85·7; H, 6·2%).

Di-β-*naphthylvinyl ketone*, $CO(CH{:}CH{\cdot}C_{10}H_7)_2$, which was only

* This substance crystallised from alcohol, in which it was somewhat sparingly soluble, in colourless prisms, m. p. 171° (Found: N, 5·8. $C_{17}H_{13}ON$ requires N, 5·7%).

formed in traces when the condensation of β-naphthaldehyde and acetone was carried out under the above-mentioned conditions, formed the main product of the reaction when a solution of the aldehyde in acetone was treated with a drop of a sodium methoxide solution. It was very sparingly soluble in most of the ordinary organic solvents, but crystallised from hot toluene in fine, sulphur-yellow needles, m. p. 241° (Found : C, 89·5; H, 5·6. $C_{25}H_{18}O$ requires C, 89·8; H, 5·4%).

2-*γ-Oximinobutenylnaphthalene*, prepared by treating the corresponding ketone with hydroxylamine hydrochloride and sodium acetate in absolute-alcoholic solution, crystallised from methyl alcohol in glistening plates, m. p. 158—160°. Indications of the presence of an isomeride in the mother-liquor were obtained, but this was not isolated in a pure state (Found : C, 79·7; H, 6·6. $C_{14}H_{13}ON$ requires C, 79·6; H, 6·2%).

2-*γ-Ketobutylnaphthalene* was readily obtained in a quantitative yield when the unsaturated ketone, suspended in acetic acid, was reduced, in the presence of colloidal platinum, by hydrogen under a pressure of 2 atmospheres. It was a somewhat viscous, colourless oil, b. p. 180—182°/8 mm. In alcoholic solution it gave no colour with ferric chloride (Found : C, 84·6; H, 7·3. $C_{14}H_{14}O$ requires C, 84·8; H, 7·1%). The *oxime* crystallised from methyl alcohol in long, glistening needles, m. p. 129° (Found : N, 6·8. $C_{14}H_{15}ON$ requires N, 6·6%). The *semicarbazone* separated from methyl alcohol in small prisms, m. p. 161—162° (Found : N, 16·6. $C_{15}H_{17}ON_3$ requires N, 16·5%).

1-*Methyl*-3 : 4-*dihydro*-α-*naphthaisoquinoline* (XV).—A mixture of the oxime (6 g.), toluene (60 c.c.), and phosphorus pentoxide (10 g.) was boiled with constant agitation for 30 minutes; phosphorus pentoxide (10 g.) was again added and the heating continued for 1 hour. The toluene was decanted from the cooled reaction mixture, and the phosphorus pentoxide dissolved in ice water; a considerable quantity of red tar then separated. The aqueous extract, which had a blue fluorescence, was separated, extracted with ether to remove any neutral products, and basified with potassium hydroxide solution. The thick, colourless oil that separated was extracted with ether, and the ethereal solution dried and evaporated (yield 1·2 g.). The crude oily base was dissolved in alcohol and treated with the calculated quantity of an alcoholic solution of picric acid; the *picrate*, which separated in sparingly soluble, yellow prisms, was recrystallised from acetone; it decomposed at 207—208° (Found : C, 56·8; H, 4·4; N, 13·3. $C_{20}H_{16}O_7N_4$ requires C, 56·9; H, 3·8; N, 13·2%). The *base* regenerated from the picrate solidified when cooled in a freezing mixture. It had m. p.

36—37°, and this m. p. was unchanged by crystallisation from dilute methyl alcohol, from which the base separated in glistening leaflets, containing apparently a molecule of methyl alcohol of crystallisation (Found : C, 79·8; H, 7·1. $C_{14}H_{13}N,CH_3{\cdot}OH$ requires C, 79·3; H, 7·4%).

4-*Methyl*-1 : 2-*dihydro*-β-*naphtha*isoquinoline (XIV). — The α-naphthaldehyde was prepared from α-*naphthanilide* * under exactly similar conditions to those used for the preparation of β-naphthaldehyde (yield 75%).

1-γ-*Ketobutenylnaphthalene* was prepared in a similar manner to the 2-isomeride (p. 2257). It was obtained as a pale yellow, uncrystallisable oil, b. p. 200—201°/10 mm. (Found : C, 85·2; H, 5·9. $C_{14}H_{12}O$ requires C, 85·7; H, 6·2%).

1-γ-*Oximinobutenylnaphthalene* crystallised from methyl alcohol in small nodules, m. p. 136—137° (Found : N, 6·6. $C_{14}H_{13}ON$ requires N, 6·6%).

1-γ-*Ketobutylnaphthalene*, readily obtained by the reduction of the unsaturated ketone with hydrogen in the presence of colloidal platinum, was a colourless, mobile oil, b. p. 192—195°/17 mm., having a pleasant smell reminiscent of acetophenone (Found : C, 84·8; H, 7·1. $C_{14}H_{14}O$ requires C, 84·8; H, 7·1%). The *oxime* crystallised from light petroleum (b. p. 60—80°) in long, glistening needles, m. p. 96—97°. It was readily soluble in most of the usual organic solvents (Found : N, 7·0. $C_{14}H_{15}ON$ requires N, 6·6%).

4-*Methyl*-1 : 2-*dihydro*-β-*naphtha*isoquinoline was obtained from the oxime by the method employed for the preparation of the isomeride (p. 2258). After removal of the ether, the base crystallised immediately in colourless needles which darkened rapidly on exposure to air. It crystallised from dilute acetone in glistening needles, m. p. 101—102° (Found : N, 7·2. $C_{14}H_{13}N$ requires N, 7·2%). It was very readily soluble in all the ordinary organic solvents, but insoluble in water. In benzene solution it showed a marked blue fluorescence, which was also shown in other solvents but in a less marked degree. The hydrochloride was very readily soluble in water, and the solution gave, on the addition of platinic chloride, a very sparingly soluble chloroplatinate, which separated as a brown, microcrystalline powder. The *picrate* crystallised from a large volume of alcohol or acetone, in both of which solvents it is very sparingly soluble, in fine, sulphur-yellow needles which darkened at 214° and decomposed at 221° (Found : C, 56·8; H, 4·4. $C_{20}H_{16}O_7N_4$ requires C, 56·9; H, 3·8%).

* α-*Naphthanilide* crystallised from alcohol in prisms, m. p. 162—163° (Found : N, 5·8. $C_{17}H_{13}ON$ requires N, 5·7%).

We wish to express our thanks to Messrs. Windle and Bhagvat for carrying out several of the analyses, to Mr. S. Narayan Iyer for his help with the catalytic reductions, and to the Government Grant Committee of the Royal Society for a grant which has defrayed part of the expense of this investigation.

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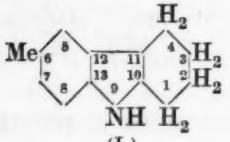
CCXCVIII.—*Derivatives of Tetrahydrocarbazole. Part VI. Compounds Derived from* 6-*Methyltetrahydrocarbazole.*

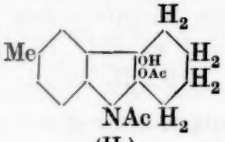
By BASAVALINGAIAH LINGAIAH MANJUNATH and SYDNEY GLENN PRESTON PLANT.

THIS investigation was undertaken with a view to study the possibility of obtaining, from a derivative of tetrahydrocarbazole which contains a substituent in the benzenoid part of the molecule, a series of compounds similar to those obtained from tetrahydrocarbazole by Perkin and Plant (J., 1923, **123**, 676), and for this purpose 6-methyltetrahydrocarbazole (I) was selected.

This substance was prepared from *p*-tolylhydrazine and *cyclo*hexanone by Fischer's method for synthesising indole derivatives (compare Borsche, Witte, and Bothe, *Annalen*, 1908, **359**, 62). Its 9-*acetyl* derivative, on treatment with nitric acid in glacial acetic acid solution, gave three substances, *viz.*, a nitro-compound, presumably 5-*nitro*-9-*acetyl*-6-*methyltetrahydrocarbazole*, and 9-*acetyl*-10 : 11-*dihydroxy*-6-*methylhexahydrocarbazole*, corresponding to the products of Perkin and Plant, and also a compound, $C_{17}H_{21}O_4N$, which appears to be 9-*acetyl*-10-*acetoxy*-11-*hydroxy*-6-*methylhexahydrocarbazole* (II). An isomeric structure (III) is possible for this derivative, but (II) is considered to be the more probable. The latter two substances, on treatment with potassium hydroxide, gave the same bright yellow product, $C_{13}H_{15}ON$, apparently 11-*hydroxy*-6-*methyltetrahydrocarbazolenine*, which, like 11-hydroxytetrahydrocarbazolenine, gives a colourless *acetyl* derivative (IV).



(I.)



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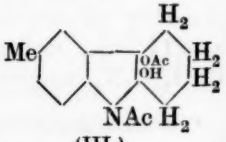
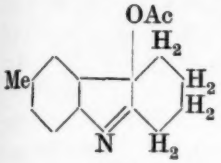
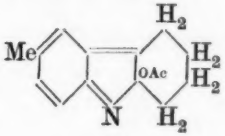


(III.)

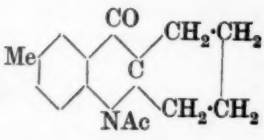
9-Acetyl-10-acetoxy-11-hydroxy-6-methylhexahydrocarbazole, on treatment with sodium hydroxide under rather different conditions, gave a bright orange-red substance, $C_{15}H_{17}O_2N$, which on account of its colour is probably 10-*acetoxy*-6-*methyltetrahydrocarbazolenine* (V), being isomeric with the colourless acetyl derivative of 11-hydroxy-6-methyltetrahydrocarbazolenine.



(IV.)



(V.)



(VI.)

Attempts to prepare 6-*acetyl*-9-*methyl*-ψ-*indoxyl*spirocyclo*pentane* from 9-acetyl-10 : 11-dihydroxy-6-methylhexahydrocarbazole gave products which could not be crystallised, but 9-acetyl-10-acetoxy-11-hydroxy-6-methylhexahydrocarbazole, on heating, gave acetic acid and a substance, $C_{15}H_{17}O_2N$, which appears to be the desired compound (VI).

The action of nitric acid on 9-*benzoyl*-6-*methyltetrahydrocarbazole* has been investigated, but the products have not been obtained crystalline.

Experimental.

9-*Acetyl*-6-*methyltetrahydrocarbazole*.—6-Methyltetrahydrocarbazole, prepared by warming *cyclo*hexanone-*p*-tolylhydrazone with dilute sulphuric acid (Borsche, Witte, and Bothe, *loc. cit.*), was boiled with acetic anhydride (3 parts) for 3 hours. The product which separated on cooling, after being washed with acetic acid and with alcohol, was pure 9-*acetyl*-6-*methyltetrahydrocarbazole* (yield 75%). It separated from glacial acetic acid in colourless prisms, m. p. 145° (Found : N, 6·3. $C_{15}H_{17}ON$ requires N, 6·2%).

Action of Nitric Acid on 9-*Acetyl*-6-*methyltetrahydrocarbazole*.—The tetrahydrocarbazole (18 g.) was dissolved in glacial acetic acid (45 c.c.) at 80°, and nitric acid (5·2 c.c.; *d* 1·42), dissolved in acetic acid (12 c.c.), was added gradually with vigorous stirring, the temperature rising to 105° and nitrous fumes being evolved. The product, which separated slowly on frequent rubbing, after being washed with a little alcohol, melted at 150—200° (yield 6 g.). It was dissolved in hot alcohol (750 c.c.), and from the filtered solution long, yellow needles (3 g.) of 5-*nitro*-9-*acetyl*-6-*methyltetrahydrocarbazole*, m. p. 165°, slowly separated (Found : N, 10·4. $C_{15}H_{16}O_3N_2$ requires N, 10·3%). The filtrate from this solution on being stirred, slowly deposited small, colourless prisms (2 g.), m. p. 220°, of

9-acetyl-10 : 11-dihydroxy-6-methylhexahydrocarbazole (Found : C, 68·6; H, 7·3; N, 5·6. $C_{15}H_{19}O_3N$ requires C, 68·9; H, 7·3; N, 5·4%). Like 9-acetyl-10 : 11-dihydroxyhexahydrocarbazole, it is coloured red by sulphuric acid and dissolves to give a yellow solution.

In some experiments the alcoholic filtrate from the 5-nitro-9-acetyl-6-methyltetrahydrocarbazole, on being stirred, slowly deposited an entirely different product consisting of colourless prisms, m. p. 210°. Analysis suggested that this substance is *9-acetyl-10-acetoxy-11-hydroxy-6-methylhexahydrocarbazole* (Found : C, 67·2; H, 7·0; N, 4·6. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 6·9; N, 4·6%), and like the above derivative it is coloured red by sulphuric acid and dissolves to give a yellow solution. The formation of this derivative was assisted by using a suspension of 9-acetyl-6-methyltetrahydrocarbazole in acetic acid at 50°, only a small amount of the nitro-compound then being formed.

The acetyl group was removed from 5-nitro-9-acetyl-6-methyltetrahydrocarbazole by boiling it with potassium hydroxide in aqueous alcohol for an hour. *5-Nitro-6-methyltetrahydrocarbazole*, obtained on diluting the solution with water, crystallised from alcohol in large, brown plates, m. p. 181—182° (Found : N, 12·1. $C_{13}H_{14}O_2N_2$ requires N, 12·2%).

Action of Potassium Hydroxide on 9-Acetyl-10 : 11-dihydroxy-6-methylhexahydrocarbazole.—A deep red solution was produced on boiling the dihydroxy-derivative (3 g.) with alcohol (45 c.c.) and a solution of potassium hydroxide (10 g.) in water (30 c.c.). After ½ hour, it was poured into cold water, and the sticky solid precipitated was crystallised from light petroleum; *11-hydroxy-6-methyltetrahydrocarbazolenine* then separated in long yellow needles, m. p. 130° (Found : C, 77·8; H, 7·4; N, 7·3. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·4; N, 7·0%). This substance shows properties similar to those of 11-hydroxytetrahydrocarbazolenine (Perkin and Plant, *loc. cit.*). Its solution in methyl alcohol shows a strong fluorescence, which is destroyed on addition of a drop of ferric chloride.

The substance was boiled with an excess of acetic anhydride for 2 hours, and the solution shaken with a large bulk of water. The *11-acetoxy-6-methyltetrahydrocarbazolenine* thus obtained crystallised from petroleum in colourless prisms, m. p. 116—117° (Found : C, 74·5; H, 7·1; N, 5·8. $C_{15}H_{17}O_2N$ requires C, 74·1; H, 7·0; N, 5·7%).

Action of Alkalis on 9-Acetyl-10-acetoxy-11-hydroxy-6-methylhexahydrocarbazole.—On treating 9-acetyl-10-acetoxy-11-hydroxy-6-methylhexahydrocarbazole with potassium hydroxide under the conditions described above, 11-hydroxy-6-methyltetrahydrocarbazolenine was again the product obtained, but when the substance

(3 g.) was boiled with alcohol (45 c.c.) and a solution of sodium hydroxide (10 g.) in water (25 c.c.), a deep red solution was obtained, which, on dilution with water, yielded a sticky solid. This, after being crystallised twice from petroleum, was obtained in orange-red needles (0·3 g.), m. p. 79°. It has been suggested (p. 2261) that this product is 10-*acetoxy*-6-*methyltetrahydrocarbazolenine* (Found: C,73·8; H, 7·1; N, 5·8. $C_{15}H_{17}O_2N$ requires C, 74·1; H, 7·0; N, 5·7%).

Action of Heat on 9-*Acetyl*-10-*acetoxy*-11-*hydroxy*-6-*methylhexahydrocarbazole.*—When this hexahydrocarbazole derivative (10 g.) was heated for a minute at 240° it decomposed, acetic acid being evolved. The residue was distilled and the oil, b. p. 220—240°/13 mm., was crystallised several times from petroleum; colourless needles (0·3 g.) of 6-*acetyl*-9-*methyl*-ψ-*indoxyl*spirocyclo*pentane*, m. p. 174°, were thus obtained (Found: C, 74·5; H, 7·1; N, 5·8. $C_{15}H_{17}O_2N$ requires C, 74·1; H, 7·0; N, 5·7%).

9-*Benzoyl*-6-*methyltetrahydrocarbazole.*—Magnesium (4·8 g.) was dissolved in a mixture of ethyl iodide (32 g.) and dry ether (450 c.c.), and 6-methyltetrahydrocarbazole (37 g.) was gradually added. A vigorous reaction took place with the evolution of ethane and the formation of 6-*methyltetrahydrocarbazyl*-9-*magnesium iodide*, and it was completed by warming for a few minutes. Benzoyl chloride (28·5 g.) was then added in small quantities at a time; much heat was evolved and a heavy viscous layer separated. After some time, the mixture was treated with ice and water, the ethereal layer shaken with dilute hydrochloric acid and dried over calcium chloride, and the ether removed. The oily residue was dissolved in boiling alcohol with the addition of animal charcoal, and, after filtration, 9-*benzoyl*-6-*methyltetrahydrocarbazole* separated, on cooling, in colourless prisms, m. p. 118° (yield 50%) (Found: N, 4·8. $C_{20}H_{19}ON$ requires N, 4·8%). Attempts to obtain a crystalline product by the interaction of 9-benzoyl-6-methyltetrahydrocarbazole with nitric acid under various conditions were unsuccessful.

The authors wish to express their thanks to Mr. F. C. Hall for carrying out the analyses given in this paper.

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CCXCIX.—2 : 2′-*Bis*-1 : 3-*benzdithiolene.*

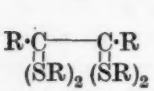
By WILLIAM ROBERT HARDY HURTLEY and SAMUEL SMILES.

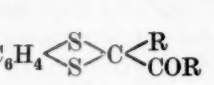
IN a previous communication (Hurtley and Smiles, this vol., p. 1821) dealing with the production of five-membered ring systems from

o-dithiolbenzene, the formation and properties of derivatives of 1 : 3-benzdithiole were studied. The experiments now described comprise a further study of the formation of cyclic systems from this dithiol, attention being mainly directed to the conditions of formation and stability of the bis-1 : 3-benzdithiole system.

Posner (Ber., 1902, **35**, 506) has shown that 7 : 7′-dithioaryl derivatives of stilbene are formed during the interaction of benzoin and mercaptans. The mechanism of this reaction does not seem at all clear, but since both aromatic and aliphatic mercaptans appear readily to take part in it, it was expected that *o*-dithiolbenzene and benzoin would yield 2 : 3-diphenyl-1 : 4-benzdithien. However, in spite of repeated trial, the formation of this substance containing the six-membered ring has not yet been realised in this manner.

o-Dithiolbenzene and αβ-dithiolethane [dithioethyleneglycol] also differ from the monothiols in their behaviour with diketones. With the monothiols the formation of dimercaptols (I) from α-diketones has been recorded (Posner, *Ber.*, 1900, **33**, 2983; 1902, **35**, 493), but with the dithiols mentioned the reaction of the second carbonyl group under similar conditions has not yet been observed, the product in


(I.)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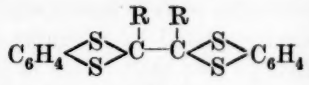
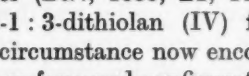
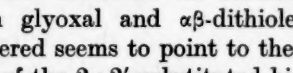

(III.)

all the cases examined being of the monomercaptol type (II). Fasbender (*Ber.*, 1888, **21**, 1473) has described the formation of 2 : 2′-bis-1 : 3-dithiolan (IV) from glyoxal and αβ-dithiolethane, but the circumstance now encountered seems to point to the instability or unfavoured configuration of the 2 : 2′-substituted bis-1 : 3-dithiole system (for example, III), and it is worth noting that a similar character has been observed with analogous derivatives of other heterocyclic systems (J., 1924, **125**, 878). It is also remarkable that only the monomercaptol (V) has been isolated from the reaction of *o*-dithiolbenzene with acetylacetone.

(IV.) 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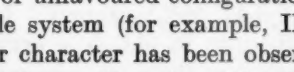
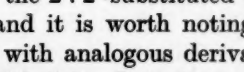
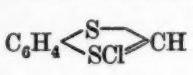
(VI.) 


(VII.)

Since the unsaturated derivatives of the required type are generally endowed with great stability, the formation of 2 : 2′-bis-1 : 3-benzdithiolene (VI) was sought. From the interaction of tetrachloroethylene and *o*-dithiolbenzene a substance of the anticipated properties, such as high melting point and volatility, was isolated;

but this method of formation permits no decision between the alternative structures (VI and VII) containing the five- and six-membered systems respectively. Evidence for the constitution of the substance was obtained as follows.

As previously shown (Hurtley and Smiles, *loc. cit.*) in the case of the 2-phenyl derivative, the 2-hydroxy-derivatives of the 1 : 3-benzdithiole system behave as pseudo-bases and are converted by acids into the salts of 1 : 3-benzdithiylium. Accordingly, from *o*-dithiolbenzene and ethyl orthoformate in presence of hydrogen chloride deeply coloured solutions of the 1 : 3-benzdithiylium 1-chloride were obtained (VIII). This salt was not isolated owing to its high solubility, but it was obtained as the crystalline *chloroplatinate* and *zinc chloride* double salt. As in the case of the 2-phenyl



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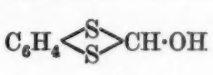

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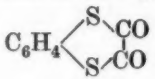
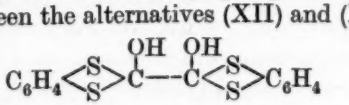


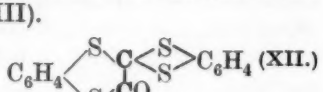
(X.)

derivative, the salts of 1 : 3-benzdithiylium are readily hydrolysed, yielding the pseudo-base, and when the zinc chloride double salt is treated with warm acetic anhydride the pseudo-base (IX) at first liberated suffers dehydration and 2 : 2′-*bis*-1 : 3-*benzdithiolene* (VI) is formed; this product is identical with that obtained from tetrachloroethylene.

Derivatives of this substance are formed in the reaction of oxalyl chloride with *o*-dithiolbenzene. With excess of oxalyl chloride in a suitable solvent the unstable yellow *oxalyl* derivative (X) containing the 1 : 4-benzdithian system is formed, but with excess of the dithiol under carefully regulated conditions a colourless product is formed of entirely different character. The instability of this material prevented isolation in a state suitable for analysis, but the behaviour of the substance clearly shows that it contains the 2 : 2′-bis-1 : 3-benzdithiole system and that it must be regarded as the 2 : 2′-dihydroxy-derivative of this (XI). For example, even when kept in neutral solvents it spontaneously yields among other products 2 : 2′-bis-1 : 3-benzdithiolene (VI). In its capacity of an α-ditertiary alcohol the substance (XI) is sensitive to acid reagents. The stable colourless product then formed does not exhibit the reactions of the thionyl group and for its structure the choice lies between the alternatives (XII) and (XIII).

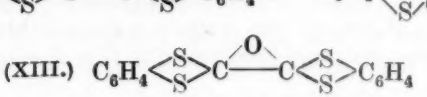
(XI.)





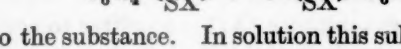
(XII.)

(XIII.)



The latter (XIII), containing the ethylene oxide ring, must be discarded, since the substance is not attacked by warm hydrogen chloride and does not yield thiylium salts like other 2-oxides of this series. Moreover, the former alternative (XII) is confirmed by the synthesis from the oxalyl derivative (X) and *o*-dithiolbenzene. It is evident that the structure (XI) assigned to the substance yielded by oxalyl chloride and excess of the dithiol accords well with its conversion in acid media into this *spiro*-derivative (XII), which appears to be the result of a pinacolinic change, the case being similar to that of the formation of 10 : 10-diphenylenephenanthrone (Klinger and Lonnes, *Ber.*, 1896, **29**, 2152; Werner and Grot, *Ber.*, 1904, **37**, 2894) during the oxidation of bisdiphenylene-ethylene in presence of acid. Attention may also be directed to the interesting fission which the *spiro*-derivative suffers when heated. At about 200—250°, a smooth decomposition ensues, 1 : 3-benzdithiole-2-one and 2 : 2′-bis-1 : 3-benzdithiolene (VI) being formed. This process, involving a redistribution of the molecule, may be ascribed to the relative instability of the six-membered ring system previously observed in the case of the simple oxalyl derivative.

Finally, it must be remarked that a substance possessing the 2 : 2′-dihydroxy-structure (XI) should under suitable conditions show the character of a pseudo-base in common with other 2-hydroxy derivatives. This condition is fulfilled by the substance in question, since treatment with sulphuric acid in acetic anhydride produces from it a deep purple, crystalline *sulphate*. This salt is rapidly hydrolysed by water, the chief product being the *spiro*-derivative, whilst in presence of ammonia 2 : 2′-bis-1 : 3-benzdithiolene is formed; these substances are the characteristic decomposition products of the pseudo-base (XI) under acid and neutral conditions respectively. Reduction of the sulphate furnished the last-named substance. These reactions indicate that the salt contains the bis-1 : 3-benzdithiole skeleton and that the pseudo-base is regenerated from it by hydrolysis; the dithiylium structure (XIV) is therefore


(XIV.)

assigned to the substance. In solution this sulphate is stable only in presence of excess of acid; it separates from the medium as a complex sulphate of the type $2BSO_4,H_2SO_4$ and it is worth notice that similar behaviour was observed (Hurtley and Smiles, *loc. cit.*) with the chloride of 2-phenyl-1 : 3-benzdithiylium, which was isolated as the complex 2BCl,HCl. 2 : 2′-Bis-1 : 3-benzdithiolene absorbs four atomic proportions of iodine; the product is remarkably stable and it is doubtful whether it should be assigned to this class of dithiylium salts.

EXPERIMENTAL.

2-Acetyl-2-methyl-1:3-benzdithiole (II).—A solution of diacetyl (1 mol.) and *o*-dithiolbenzene (2 mols.) in alcohol was saturated with dry hydrogen chloride at the ordinary temperature. The compound (II) (yield 80—85%), separation of which began in a few minutes, was sparingly soluble in the usual organic media and crystallised from hot alcohol in colourless plates, m. p. 156° (Found: C, 57·3; H, 4·7. $C_{10}H_{10}OS_2$ requires C, 57·1; H, 4·8%).

With equimolecular proportions of the reagents poor yields of this product were obtained. Similar experiments with αβ-dithiolethane and diacetyl showed that the mercaptan was oxidised by the diketone. Posner (*Ber.*, 1902, **35**, 493) has recorded a similar action of diacetyl with phenyl mercaptan.

2-Benzoyl-2-phenyl-1:3-benzdithiole (II).—A solution of benzil (1·5 g.) and *o*-dithiolbenzene (1 g.) in alcohol (25 c.c.) was saturated at 5° with dry hydrogen chloride. The required product was collected (90—95% yield) after 15 minutes; it separated from hot alcohol in pale yellow needles, m. p. 175° (Found: C, 71·7; H, 4·5. $C_{20}H_{14}OS_2$ requires C, 71·8; H, 4·2%).

2-Benzoyl-2-phenyl-1:3-dithiolan, $\begin{matrix}CH_2{\cdot}S\\ CH_2{\cdot}S\end{matrix}\!>\!CPh{\cdot}COPh$, was prepared (80% yield) in a similar manner from a solution of benzil (2 g.) and αβ-dithiolethane (0·9 g.) in alcohol (15 c.c.) It separated from hot alcohol in needles, m. p. 94—95° (Found: C, 66·7; H, 5·2; *M*, 276. $C_{16}H_{14}OS_2$ requires C, 67·1; H, 4·9%; *M*, 286).

2-Acetonyl-2-methyl-1:3-benzdithiole (V).—Acetylacetone (1 mol.) was added to a solution of *o*-dithiolbenzene (2 mols.) in alcohol (15 parts). After the mixture had been saturated with hydrogen chloride at 5°, the required mercaptol (60—65% yield) separated in colourless needles which, after purification, had m. p. 119° and gave a purple solution in sulphuric acid (Found: C, 59·1; H, 5·2. $C_{11}H_{12}OS_2$ requires C, 58·9; H, 5·4%). When equimolecular proportions of the reagents were used, no mercaptol could be isolated; the resinous product contained the disulphide.

1:3-Benzdithiylium 1-Chloride (VIII).—A mixture of *o*-dithiolbenzene (1·5 g.), ethyl orthoformate (1·6 g.), and alcohol (10 c.c.) was saturated at 5° with hydrogen chloride. After 15 hours, the orange-brown solution was mixed with powdered anhydrous zinc chloride, which rapidly dissolved. The crystals of the *zinc chloride* double salt of the required substance which separated were washed with alcohol and then with ether; the orange needles thus obtained had in most preparations a red tint of varying depth. The material could not be recrystallised (Found: Zn, 13·0. $2C_7H_5ClS_2,ZnCl_2$ requires Zn, 12·7%). The *chloroplatinate* was obtained in glistening

orange prisms by adding aqueous chloroplatinic acid to a solution of this zinc chloride double salt in excess of concentrated hydrochloric acid [Found: C, 23·4; H, 1·6; Pt, 27·2. $(C_7H_5S_2)_2PtCl_6$ requires C, 23·5; H, 1·4; Pt, 27·3%]. The substance darkens at about 220°.

When a solution of αβ-dithiolethane (1 g.) and ethyl orthoformate (2 g.) in alcohol (20 c.c.) was saturated with hydrogen chloride, *ethylene trithioformate* (1·1 g.) rapidly separated; it formed needles, m. p. 104—105°, from hot alcohol (Found: C, 31·9; H, 4·9. $C_8H_{14}S_6$ requires C, 31·8; H, 4·6%). The behaviour of this aliphatic dithiol with the orthoformate is similar to that of ethyl mercaptan, which yields trimethyl orthothioformate (Holmberg, *Ber.*, 1907, **40**, 1740).

The interaction of oxalyl chloride and *o*-dithiolbenzene leads to different products according to the conditions.

(*a*) 1 : 4-Benzdithian-2 : 3-dione. Oxalyl chloride (4 g.; an excess) was carefully added to a solution of *o*-dithiolbenzene (2 g.) in dry acetone (60 c.c.). After 5 minutes, when the vigorous reaction had subsided, the greater part (about 55 c.c.) of the solvent was evaporated.

1 : 4-*Benzdithian*-2 : 3-*dione* (X) separated (0·7 g.) from the cooled residue; it was purified by rapid treatment with warm benzene from which it separated in bright yellow prisms, m. p. 160° (decomp.). It was decomposed by boiling water, alcohol, or acetic acid and quickly dissolved by aqueous alkali hydroxide (2*N*). A resinous material was slowly deposited from the cold solution in benzene (Found: C, 49·0; H, 2·0; *M*, 192. $C_8H_4O_2S_2$ requires C, 48·9; H, 2·1%; *M*, 196).

(*b*) With excess of *o*-dithiolbenzene and without a solvent, derivatives of 2 : 2′-bis-1 : 3-benzdithiole or the spiro-*compound* (XII) are formed. Oxalyl chloride was added to twice its weight of the dithiol and when evolution of hydrogen chloride had almost ceased the mixture was warmed on the water-bath for about ¼ hour. The more soluble part was extracted from the cooled mass with ether, and the solvent rapidly removed at the ordinary temperature. The crystalline residue, which exhibited the properties of 2 : 2′-dihydroxy-bis-1 : 3-benzdithiole (XI), could not be purified by the usual methods; the yield varied considerably according to the conditions of interaction, which were somewhat difficult to control with the small amounts of reagents available. A solution in benzene was allowed to evaporate spontaneously, and 2 : 2′-bis-1 : 3-benzdithiolene (VI) was isolated from the residue. A warm dilute solution of the substance in acetic anhydride was mixed with concentrated sulphuric acid (about 16 drops in 100 c.c. of solution)

and kept for 12 hours. 2 : 2′-*Bis*-1 : 3-*benzdithiylium sulphate* was then precipitated in the crystalline state. The yield varied, but was usually about 0·9 g. from 2 g. of the dithiol. The salt was dissolved in hot dilute sulphuric acid (60%), and separated from the cold medium in long, deep purple needles which exhibited a bronze lustre and had m. p. 268—270° (decomp.) (Found: C, 35·8; H, 2·7; SO_4, 31·2, 31·0. $2C_{14}H_8S_4{\cdot}SO_4$, $H_2SO_4{,}2H_2O$ requires C, 36·0; H, 2·35; SO_4, 30·8%).

Reduction of this sulphate in 60% sulphuric acid with zinc dust yielded 2 : 2′-bis-1 : 3-benzdithiolene, and the same substance was isolated from the product formed on hydrolysis with warm, dilute ammonia. The permanganate-coloured aqueous solution of the salt was rapidly decolorised by boiling; hydrolysis under these weakly acid conditions gave a mixture of 2 : 2′-bis-1 : 3-benzdithiolene and 3-*keto*-1 : 4-*benzdithian*-2 : 2′-spiro-1′ : 3′-*benzdithiole* (XII).

The latter substance (XII) was more conveniently prepared directly from the interaction of oxalyl chloride and *o*-dithiolbenzene by prolonging the period of warming and extracting the residue with hot acetic acid. The material (1·3 g. from 2 g. of the dithiol) was isolated by diluting the extract with water and, after purification from acetone with the aid of charcoal, was obtained in short needles, m. p. 168°, which gave an orange solution with concentrated sulphuric acid. It was also obtained by boiling the acetic acid solution of the more soluble product which is formed under milder conditions. This substance seems always to be formed to some extent in the reaction of oxalyl chloride with the dithiol and under the conditions described forms the greater portion of the product. It was synthesised by warming equal weights of the oxalyl derivative (X) and the dithiol on the water-bath. The product was kept for 12 hours and then treated with ether in presence of aqueous sodium hydroxide. Evaporation of the solvent yielded the required material, which was purified and identified in the usual manner (Found: C, 52·8; H, 2·9; S, 39·9; *M*, 312. $C_{14}H_8OS_4$ requires C, 52·5; H, 2·5; S, 40·0%; *M*, 320).

2 : 2′-*Bis*-1 : 3-*benzdithiolene* (VI) was obtained by several methods. (*a*) Decomposition of the substance (XII) described in the preceding paragraph began slightly above the melting point, but was rapid at 200° and above. 1 : 3-Benzdithiole-2-one (this vol., p. 1826) was isolated by distillation in steam and identified in the usual manner, whilst the residue, purified from benzene, yielded the desired substance (0·7 g. from 3 g. of material).

(*b*) A solution of the dithiol (4 g.) and tetrachloroethylene (2·3 g.) in alcohol (15 c.c.), in which the requisite amount of sodium had been

dissolved, was kept in a sealed tube at 110—120° for 7 hours. The yellow material obtained after the unchanged dithiol had been removed was purified from benzene (yield 0·5 g.).

(c) The zinc chloride double salt of 1 : 3-benzdithiylium (VIII) was added to boiling acetic anhydride. When the action was complete, the solid was separated from the cooled liquid and purified as usual (yield about 30%).

The substance is also formed by alkaline hydrolysis or by reduction of the dithiylium sulphate and in the spontaneous decomposition of the pseudo-base obtained from oxalyl chloride and the dithiol. It is sparingly soluble in the usual organic media and is obtained from benzene in golden needles, m. p. 234°, which volatilise when heated (Found: C, 55·1; H, 2·9; *M*, 291. $C_{14}H_8S_4$ requires C, 55·3; H, 2·6%; *M*, 296). It is oxidised by sulphuric acid, the purple dithiylium sulphate being formed; and when a benzene solution of iodine was added to a similar solution of the substance a *tetra-iodo*-additive product was precipitated as a finely-divided black powder (Found: I, 63·0. $C_{14}H_8I_4S_4$ requires I, 62·7%). This substance was remarkably stable and was unattacked by aqueous alkali hydroxide or by aqueous potassium iodide.

In conclusion, we desire to express our thanks to the Department of Scientific and Industrial Research for a grant which has enabled one of us to take part in these experiments.

KING'S COLLEGE, LONDON. [*Received, June 17th*, 1926.]

CCC.—*The Interaction of Sulphur Dioxide and Hydrogen Sulphide.*

By ERNEST MATTHEWS.

Interaction in the Gaseous State.

IT has long been known that dry gaseous hydrogen sulphide and sulphur dioxide do not interact on mixing, but that they will react in the presence of water and certain other liquids. It has been suggested that there might be some relationship between the dielectric constant for a given substance and its ability or inability to cause the mutual decomposition of the two gases. Thus, Klein (*J. Physical Chem.*, 1911, **15**, 15) says: "While the dependence of chemical activity on the dielectric constant is not expressly stated by Baker in the Wilde Lecture for 1909, yet it is certainly implied." As a result of his own experiments and those of Kahlen-

berg and Schlundt (which proved that the Nernst-Thomson rule did not hold even qualitatively), he concludes that there is no such dependence. Klein's experiments have been repeated and extended but with substantially the same results.

The gases employed in the present experiments were dried by passage through a U-tube containing phosphorus pentoxide. The organic liquids were the purest obtainable and were dried and redistilled.

The results obtained are classified below; the dielectric constant is shown for each liquid, average values being given.

D.C.		Reaction.	*D.C.*		Reaction.
75	Water.	Immediate.	18	Methyl ethyl ketone.	After 2 mins.
56	Glycerol.	After 3 mins.			
55	Methyl sulphate.	„ 8 „	18	Benzaldehyde.	„ 8 „
39	Nitromethane.	„ 14 „	13	Benzyl alcohol.	Immediate.
39	Acetonitrile.	„ 3 „	11	*tert.*-Butyl alcohol.	„
34	Methyl alcohol.	Immediate.			
26	Ethyl alcohol.	„	6	Ethyl acetate.	After 8 mins.
24	*iso*Propyl alcohol.	„	5	Amyl acetate.	Immediate.
			7	Aniline.	„
19	*iso*Butyl alcohol.	„	6	Methyl benzoate.	After 20 mins.
17	*tert.*-Amyl alcohol.	„	5	Amyl benzoate.	„ 10 „
			5	Ethyl butyrate.	Immediate.
21	Acetone.	After 5 mins.	4	Ether.	After 8 mins.
21	Allyl alcohol.	Immediate.	—	Bornyl acetate.	Immediate.

No reaction occurred in the following solvents in 30 minutes: Nitrobenzene (36), phosphorus oxychloride (12), chlorobenzene (11), sulphuryl chloride (10), ethyl iodide (7), chloroform (5), carbon disulphide (3), carbon tetrachloride (2), benzene (2), and methyl salicylate (8).

Although the values of the dielectric constants are not known with accuracy, they serve to show that no rigid correspondence can hold between catalytic activity and dielectric constant.

In his work on the interaction of hydrogen sulphide and sulphur dioxide, Klein (*loc. cit.*) failed to differentiate between the action of liquid water and water vapour. Experiments have been carried out in which mixtures of these two gases, known to contain in the one case water vapour and in the other case ethyl alcohol vapour, were kept for more than 8 hours and 3 hours, respectively, before decomposition set in, and it was then due presumably to the formation of a liquid film on the surface of the glass. In each case addition of one drop of the liquid caused immediate separation of sulphur.

In view of this fact, the extreme precautions taken by Klein to dry both the gases and the reagents employed lose some of their significance, since the duration of his experiments rarely exceeded 2 hours.

Interaction in the Liquid State.

Quam (*J. Amer. Chem. Soc.*, 1925, **47**, 103) has asserted that sulphur dioxide reacts vigorously with liquid hydrogen sulphide, thus contradicting the earlier statement of Antony and Magri (*Gazzetta*, 1905, **35**, i, 206), who maintained that the liquefied gases require the presence of an ionising liquid to bring about reaction between them. In order to test this point, liquid hydrogen sulphide and liquid sulphur dioxide were mixed in the proportions of 2 : 1 in quantities of from 5—10 c.c., and in each case the mixture remained quite clear even when kept for 2 hours or more. The liquid on being warmed boiled away completely, leaving no residue except at the exit tube, where a deposit of sulphur was formed due to the presence of condensed water.

Experiments were then carried out with the liquid mixture of hydrogen sulphide and sulphur dioxide to determine under what conditions decomposition ensued. It was found that the addition of a little powdered sulphur had no effect, and also that ice was unable to cause the decomposition—a point of some interest.

The effect was then tried of the addition of 1—2 c.c. of the liquid mixture to small quantities of the most reactive organic liquids employed in the earlier experiments, when cooled to the temperature of solid carbon dioxide (— 78°). With ethyl alcohol, the decomposition was very vigorous, and almost equally so with amyl alcohol, amyl acetate, ether, ethyl acetate, acetone, and the other reactive substances which are liquid at this temperature. With ice, aniline, benzaldehyde, allyl alcohol, and glycerol, however, which were solid at this temperature, no decomposition occurred and the liquid remained clear (except for slight opalescence in the case of allyl alcohol, which did not increase on standing), although at the ordinary temperature, when liquid, they cause immediate decomposition.

Discussion.

It may be concluded that sulphur dioxide and hydrogen sulphide do not react with each other either in the gaseous state at the ordinary temperature or in the liquid state, except in the presence of a third substance in the liquid phase.

Further, the table on p. 2271 shows that the alcohols as a class are very active in effecting the decomposition. Moreover, it is found that ethyl alcohol is more effective even than water in bringing about decomposition. This would seem to be connected with the greater solubility of the two gases in alcohol than in water; thus 1 c.c. of alcohol at 16° dissolves 143 c.c. and 9 c.c. of sulphur

dioxide and hydrogen sulphide, respectively, whereas 1 c.c. of water at 16° dissolves only 43 c.c. and 3 c.c., respectively.

It would seem desirable to investigate the rate of reaction in the presence of each of these two liquids, as it is possible that the ratio of the rates of reaction might be closely related to the ratio of their solubilities in alcohol and in water.

Klein takes the view that the substances effective in causing decomposition are those which are capable of forming unstable compounds with one or other of the two gases.

The failure of methyl salicylate to bring about decomposition, whilst other substances such as amyl acetate, amyl benzoate, etc., are capable of doing so, is difficult to explain on this basis, since, for instance, methyl salicylate would be expected to form addition compounds more readily than methyl benzoate.

Summary.

1. To bring about the decomposition of a mixture of sulphur dioxide and hydrogen sulphide in either the gaseous or the liquid state, the addition of a third substance is necessary, and it has been demonstrated that this third substance must be in the liquid phase.

2. There is no rigid relationship between the values of the dielectric constants of substances and their chemical activity as measured by their ability to bring about the interaction of hydrogen sulphide and sulphur dioxide.

3. The assertion that hydrogen sulphide and sulphur dioxide when in a liquid state react vigorously, even when dry, has been disproved.

4. It is suggested that the activity of a substance in causing decomposition is dependent on the solubility of the two gases in the substance when liquid, or on the solubility of the solids in the liquid mixture of the two gases.

In conclusion, I desire to express my thanks to Professor H. B. Baker, F.R.S., for his constant interest and advice.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
SOUTH KENSINGTON. [*Received, June 2nd,* 1926.]

CCCI.—*The Formation of Protective Oxide Films on Copper and Brass by Exposure to Air at Various Temperatures.*

By WILLIAM H. J. VERNON.

IN the course of an investigation dealing *inter alia* with the tarnishing of copper, it was observed by the present author in 1923 that a

simple heat-treatment (even as short as one hour) of the freshly-cleaned metal at 97° produced a considerable degree of immunity from tarnishing on subsequent exposure to ordinary room conditions. Thus, whereas unheated specimens passed through a characteristic progression of interference colours, specimens so heated underwent no change of colour, and even after prolonged exposure suffered only a slight general darkening. It was then concluded that the protection was due to the formation of a thin film of oxide. Experiments have since been conducted to obtain information respecting films produced at both lower and higher temperatures, and the inquiry has also been extended by the inclusion of 60 : 40 brass.

Experimental.

The specimens were cut from sheets of high-grade electrolytic copper and 60 : 40 brass respectively, each in the annealed condition. Their dimensions were 10·0 cm. by 5·0 cm., by 1·25 mm. thick, giving an available area for oxidation of one sq. dm., except that three holes ($\frac{1}{8}$ inch diam.) were drilled in each specimen for the purpose of horizontal suspension. Sufficient material was removed by abrasion to ensure uniformity, and the final surface was prepared by means of fine emery paper ("Hubert, No. 1"). Each specimen was cleaned thoroughly by rubbing with pure cotton wool, and allowed to stand in an evacuated desiccator for weighing and heat treatment on the following day. The method of weighing was essentially the Gaussian method of exchange, with certain important refinements due to Conrady (*Proc. Roy. Soc.*, 1922, *A*, **101**, 211). The heat-treatment was conducted in an electric muffle, the specimen being freely suspended. In the main series of experiments, the time of heating was uniformly 70 minutes from the time of introducing the specimen, or approximately 1 hour at the desired temperature, which varied between 50° and 250° for copper, and between 200° and 425°, for brass. Each specimen was allowed to cool in a vacuum after heating and was re-weighed the following day.

Discussion of Results. (1) *Copper.*

Immediate Effects of Heat-treatment.—The weight-increments obtained are in Table I, together with the corresponding "temper colours." The upper temperature-limit employed (250°) was determined by the appearance of the dull grey scale indicating the end of the interference colour range. Within this range both "first-order" and "second-order" colours were observed. It should be borne in mind that these results are regulated not only by the temperature, but also by the time of heating.*

* Within the interference colour range it is reasonable to expect a parabolic relationship between thickness of film and time of exposure at any given

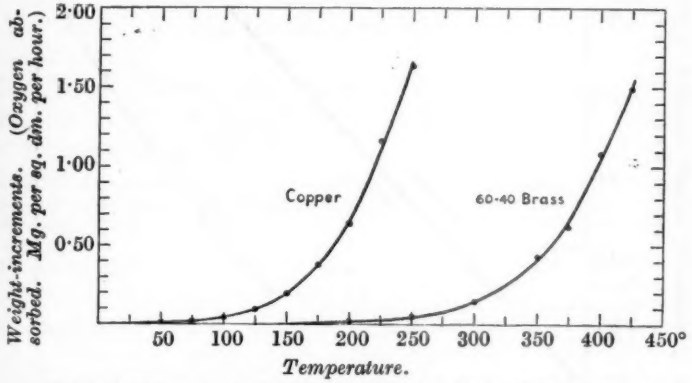
TABLE I.

Copper : Immediate effects of heat-treatment for one hour.

Temp. of heating.	Weight-increment (mg. per sq. dm.).	Change of colour.
50°	0·005	No change.
75	0·02	Merest shade darker.
100	0·04	Slightly darker but still essentially an ordinary copper colour.
125	0·095	Orange.
150	0·195	Bluish-purple.
175	0·38	Greenish-yellow.
200	0·64	Light red with tint of brown.
225	1·16	Bluish- or brownish-grey
250	1·63	Slate-grey.

In Fig. 1 weight-increments are plotted against temperature.

FIG. 1.



Weight-increments resulting from oxidation during heat-treatment.

It is of interest to compare the present results with previous quantitative work upon the oxidation of copper. So far as the author is aware, the only comparable gravimetric data are those due to Pilling and Bedworth (*J. Inst. Metals*, 1923, **29**, 529), who employed, however, considerably higher temperatures (400° to 1100°). These authors found the following empirical exponential relationship between temperature and rate of oxidation :

$$K = AT^n$$

where K = rate constant (square of weight-increment per unit area per unit time); T = absolute temperature; and A and n are constants.

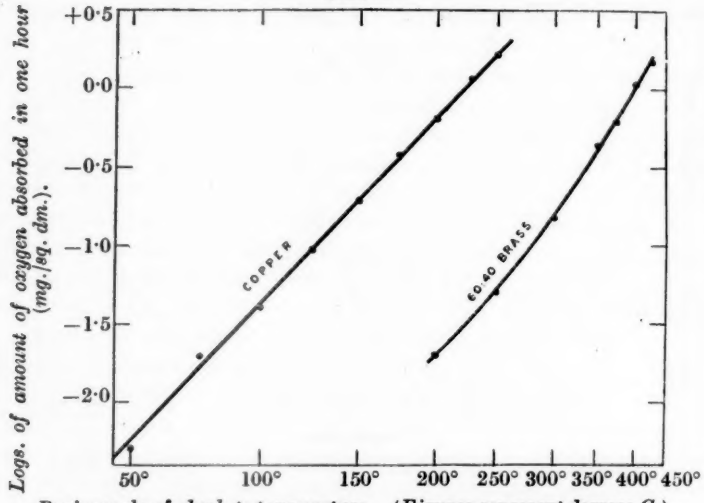
temperature. In previous work by the author (*Trans. Faraday Soc.*, 1924, **19**, 839) this relationship was found to hold for the tarnishing of copper at room temperature, and in the present experiments it has been confirmed by a series of weighings with specimens heated at 150°.

Oxide films within the interference colour range have been studied by Tammann and Köster (*Z. anorg. Chem.*, 1922, **123**, 196), who calculated from optical principles the thickness of the films giving rise to the observed colours. Their figures, however, have been criticised by Evans (*Proc. Roy. Soc.*, 1925, *A*, **107**, 234) and by Dunn (*ibid.*, 1926, *A*, **111**, 211, 217) as being based upon faulty premises. The latter author, moreover, gives a mathematical analysis of the effect of temperature upon rate of oxidation, based on the quantum theory, and deduces the equation

$$d \log W/dT = - Q/RT^2$$

which, it will be noted, is identical in form with the van 't Hoff

FIG. 2.



Reciprocals of absolute temperature. (*Figures represent degrees C.*)

Influence of temperature on rate of direct oxidation.

isochore. Here W is a *linear* function of weight-increment (compare K in previous equation), T is absolute temperature as before, and Q and R are constants. Dunn shows that this expression is in good agreement with Pilling and Bedworth's results for the high-temperature oxidation of copper, and also with his own results for certain of the zinc-copper alloys at similar temperatures.

The present results for the low-temperature oxidation of copper are approximately in agreement with Pilling and Bedworth's equation, *i.e.*, there is but little deviation from the straight line when $\log K$ is plotted against $\log T$. With Dunn's equation, however, the agreement appears to be perfect, as shown by the straight line in Fig. 2, where logarithms of weight-increment are plotted against the reciprocals of absolute temperature.

It is evident that this curve may be employed with a reasonable degree of confidence for extrapolation to atmospheric temperatures. Clearly the value of K so obtained will represent the extent of direct attack by atmospheric oxygen, and any departure from this value as observed experimentally will point to the existence of some other contributory factor under the particular conditions concerned.

Subsequent Effects of Heat-treatment.—After heat-treatment the specimens were freely suspended (together with specimens unheated but otherwise identical) in a room the atmosphere of which had previously received thorough investigation with reference to its tarnishing capacity. In its effects this atmosphere may be taken as typical of winter-time town air containing the usual traces of sulphur compounds, but free from excessive local pollution. Throughout the tests the temperature varied between the limits of 17·0° and 22·2°, and was some 14° above the dew-point during the whole time.

The visible results were particularly striking. Thus after 20 days' exposure * the appearance of a typical series of specimens may be described as follows :

1. Unheated specimen.	Tarnished a reddish-purple colour.
2. Heated at 50° (similarly for 55°).	Reddish-purple (exactly as 1).
3. Heated at 75°.	No change since heat-treatment, *i.e.*, *practically unaltered copper.*
4. Heated at 100°.	No change since heat-treatment, *i.e.*, slightly darker than 3, as result of heat-treatment, but otherwise unaltered.
5–10. Heated at 125—250°.	No change since heat-treatment, *i.e.*, colour as described in Table I.

The remarkable result thus emerges that an hour's heating in air at a temperature as low as 75°—a treatment practically without any visible effect upon the metal—is sufficient entirely to inhibit the development of interference colours on subsequent exposure to tarnishing conditions. The conclusion is inevitable that the protection is brought about by a film of oxide, either so thin as to be almost invisible (as by heating at 75°), or, while still transparent, sufficiently thick to refract light (as by heating at temperatures above 100°).

The very sudden break in behaviour between specimens heated at 55° and 75° is significant, and seems to suggest that a minimum thickness is essential if the film is to afford any protection. Interest attaches to the thickness of the films produced at these temperatures, and an estimate is therefore attempted from the available data.

* After more prolonged exposure the *visual* comparison is not so striking, since unprotected specimens assume a neutral or steely tint, and, although after this stage second-order interference colours slowly develop, the deep purple of the first order is not repeated.

Assuming the first product of interaction of copper and oxygen to be cuprous oxide (d 6·0, assumed; Landolt-Börnstein gives 5·75–6·09) the following relationships obtain for the film produced at 55°.

Weight of oxygen absorbed (from Fig. 2)	= 0·007 mg. per sq. dm.
Weight of equivalent Cu_2O	= 0·063 mg. per sq. dm.
Volume " " "	= $1·05 \times 10^{-5}$ c.c. per sq. dm.
Hence, thickness of Cu_2O film	= $1·05 \times 10^{-7}$ cm.
	= 10·5 Ångström units.

It may possibly be significant that this figure is very nearly of the same order of magnitude as that usually accepted for the lattice dimensions of cuprous oxide, *i.e.*, 4·26 Å. (see Braggs' "*X*-Rays and Crystal Structure"). Moreover, on account of the emeried nature of the surface, the *actual* area exposed to oxidation must be considerably greater than—very possibly double—the nominal area of one square decimetre which has been assumed in the calculation. Clearly, if it had been possible to employ a value more nearly approaching that of the true area, the figure obtained for the thickness of the film would have approximated even more closely to that quoted for the lattice parameter. *The suggestion emerges, therefore, that the minimum thickness of film necessary for protection may be such that the unit lattice of the oxide is completed for the whole of the surface.*

TABLE II.

Copper: Weight-increments subsequent to heat-treatment.

Temp. of heating.	Period of exposure, and increase in weight (mg. per sq. dm.). Series A. 6 Days.	34 Days.	100 Days.	Series B. 152 Days.	Series C. 206 Days.
—	0·29	0·91	1·28	1·68	2·60
50°	0·21	0·76	1·12		
75	0·00	0·30	0·42		
100	0·00	0·17	0·31	0·40	0·43
125	0·00	0·11	0·28	0·39	
150	0·00	0·15	0·24	0·34	
175				0·32	
200	0·00	0·12	0·22	0·34	
225				0·32	
250	0·00	0·19	0·26	0·33	

Weight-increments of the specimens the visible changes of which are discussed above are in Table II (Series A) and are plotted in Fig. 3. Gravimetric data for other (less complete) series after longer exposure are also included in Table II. Although protected specimens slowly increase in weight, they do not appear to undergo any further colour-change. Actually the gravimetric method does not give a satisfactory response to visible changes, and the measure-

ment of loss of reflectivity (*Trans. Faraday Soc.*, 1924, **19**, 851) is in this respect much to be preferred.

The results recorded above were obtained with specimens that had been polished with fine emery paper. Tests conducted upon a limited number of specimens brightly polished with mechanically driven "mops" yielded results which, although quite convincing gravimetrically (the figures comparing favourably with those given in Table II), were not so satisfactory from the point of view of the suppression of visible changes. In these tests, however, no other temperature than 100° was employed for the heat-treatment, and further work seems to be necessary in the case of copper polished in this way.

The Formation of Protective Oxide Films at the Ordinary Temperature.

Cleaned copper specimens exposed to room atmosphere during August–September (a period of optimum freedom from pollution) suffered no visible alteration beyond a slight general darkening. Increase in weight was determined periodically, and its relation to time shown to be parabolic. At the end of a month's exposure the mean weight-increment was 0·2 mg. per sq. dm.,* corresponding with the film produced by an hour's heating at 150°. That the agreement in physical properties was not complete is obvious from the absence of interference colours on the specimens exposed at normal temperatures. Nevertheless, it is of interest to note that once again protection was afforded, for, on subsequent exposure of such specimens to tarnishing conditions, no appreciable change was observed, whereas freshly-cleaned specimens passed through the usual progression of colours. The protection conferred by previous exposure to a relatively pure atmosphere is demonstrated by the following facts. Specimens cleaned in the ordinary way and exposed for a month to the tarnishing atmosphere increased in weight by 0·8 mg. per sq. dm. During the same time pre-exposed specimens increased by 0·06 mg. per sq. dm.; moreover, during their *whole period of exposure* they had increased by only 0·3 mg. per sq. dm.—without, of course, the accompaniment of any colour changes.

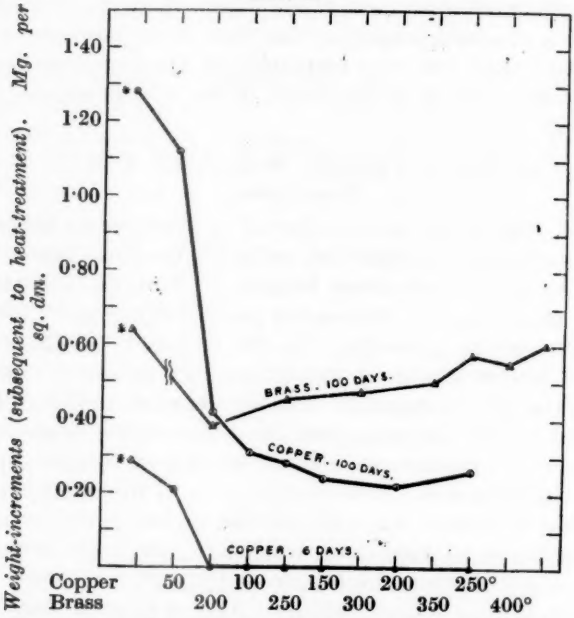
Discussion of Results. (2) 60 : 40 *Brass.*

Immediate Effects of Heat-treatment.—Weight-increments and colour-changes are recorded in Table III. As would be expected, the development of colours was not nearly so pronounced as in the case of copper. Thus, from a deepening of the original yellow

* This corresponds to a rate-constant considerably greater than that obtained by extrapolating to room temperature the straight line of Fig. 2, which demands for 1 month's exposure a weight-increment of only 0·03 mg. per sq. dm.

the metal passed directly to a neutral or "steely" stage, and attempts to obtain an intervening colour were without success. Between the neutral tint and the second-order yellow, however, an imperfect green appeared. A considerably higher temperature was required to produce a visible change than was the case with copper, *i.e.*, 200° as compared with 100°; for equivalent change of

FIG. 3.



Temperature of previous heat-treatment. (* = *not heated*).

Weight-increments resulting from tarnishing subsequent to heat-treatment.

appearance the order of weight-increment was then similar to that which had obtained for copper. At the upper limit of temperature employed (425°), specks of white zinc oxide made their appearance over the surface.

TABLE III.

60 : 40 *Brass :* Immediate effects of heat-treatment for one hour.

Temp. of heating.	Weight-increment (mg. per sq. dm.).	Change of colour.
200°	0·02	Shade darker than unheated specimen. Pale yellow.
250	0·05	Shade darker than preceding specimen.
300	0·15	Considerably darker than preceding specimen. Deep yellow.
350	0·43	Brownish-yellow.
375	0·62	"Slaty" or "steely."
400	1·08	"Steely" with greenish tint.
425	1·49	Yellow.

In Fig. 1 weight-increments are plotted against temperature, and in Fig. 2 logarithms of weight-increments against reciprocals of absolute temperature, as suggested by Dunn (*vide supra*).

It will be seen that the agreement with Dunn's equation is not so complete as in the case of copper, since there is now a slight but definite deviation from the straight line. This is not surprising in view of the more complex nature of the material and the probability of reaction between the initially formed scale and the zinc of the underlying metal. Curiously enough, however, the figures yield a straight line when log K is plotted against log T, in agreement with Pilling and Bedworth's empirical equation. The circumstance is noted, although the explanation, if any, is not obvious.

Subsequent Effects of Heat-treatment.—Available evidence as to the protective effect of oxidation is not so conclusive as that which has been recorded for copper. This is particularly true of the gravimetric results, as will be seen by reference to Fig. 3, where subsequent weight-increments of brass specimens after 100 days' exposure are plotted against the temperature of heat-treatment; corresponding data for copper are included on the same diagram. Although the first heat-treated member of the series (200°) has suffered definitely less attack than the unheated "blank," the reduction is considerably less than that which obtained for copper heated at 75°. Moreover, the weight-increment progressively increases as the temperature of heat-treatment rises (in contradistinction to the behaviour of copper) until, with the specimen heated at 250°, the increase is very little less than that suffered by the unprotected "blank." Nevertheless, the *visible results* were much more satisfactory than these figures would suggest. Thus, after 28 days' exposure untreated specimens had darkened considerably, with development of light brown patches, whilst the specimen heated at 200° had apparently undergone no change. As a result, the treated specimen appeared much lighter than the untreated blank, although when first exposed it was a shade darker owing to the effects of the heat-treatment; the remainder of the specimens appeared to have undergone no further change. After 100 days' exposure untreated specimens had become yellowish-brown generally; there was marked contrast between these and the specimen heated at 200° which was still pale yellow, whilst the remaining specimens had altered but very little in appearance since the first exposure.

It will be seen therefore that although oxide films upon brass are not so efficacious as those upon copper, there is definite evidence that the protection extends to brass, the effects being confined mainly to the suppression of further colour changes.

In the preparation of this paper and in the experimental work, respectively, the author gladly acknowledges the assistance of his colleague, Mr. J. C. Hudson, M.Sc., and of Mr. L. Whitby. For permission to publish the results his thanks are due to the Council of the British Non-ferrous Metals Research Association, whilst to Dr. R. S. Hutton (Director of the Association) he is particularly indebted for much helpful interest. The author is grateful, moreover, to Professor H. C. H. Carpenter, F.R.S., under whose general supervision the work has been conducted, and by whom important facilities have been granted.

ROYAL SCHOOL OF MINES, S.W. [*Received, July 8th*, 1926.]

CCCII.—*Acid and Salt Effects in Catalysed Reactions. Part I.*

By HARRY MEDFORTH DAWSON and JOHN STANLEY CARTER.

IN previous papers it was shown that the catalytic properties of acids cannot be interpreted in terms of the simple hydrogen-ion theory, but that an explanation of the observed effects was possible when it was assumed that catalytic activity is exhibited by the non-ionised acid as well as by the hydrogen ion.

Observations on the rate of reaction of acetone with iodine in the presence of acetic, monochloroacetic, αβ-dibromopropionic, dichloroacetic, or hydrochloric acid (Dawson and Powis, J., 1913, **103**, 2135) showed that the activity of these acids varied with the concentration in a manner which could be interpreted quite satisfactorily in terms of this theory of dual action. The results for the different acids were, moreover, shown to be consistent with one another in that the several values derived for the activity coefficient of the hydrogen ion were identical within the limits of probable error. In support of the dual theory, further evidence of a different kind was afforded by a systematic investigation of the changes produced in the catalytic activity of monochloroacetic acid by the addition of varying quantities of the corresponding sodium salt (Dawson and Reiman, J., 1915, **107**, 1426). In the aggregate, the facts established in the experiments quoted may be said to constitute a very strong case for the view that the catalytic properties of acids are not confined to the activity of the hydrogen ion.

The study of the catalytic effects of acids in presence of the corresponding salts has been continued, and some of the results obtained are here briefly described. In view of the circumstance that the primary object of the experiments was to provide further

material for analysis in terms of the dual theory and to remove possible objections to the method of interpreting the previous results, it will readily be understood that much of our experimental material is not pre-eminently adapted for the discussion of views which have been evolved since the majority of the experiments were completed.

The observations to be described refer to the catalytic action of mixtures of weak acids and their corresponding salts on the reaction between acetone and iodine at 25°. For the correlation of the reaction velocities it is essential to know as accurately as possible the hydrogen-ion concentration of the solutions employed, and here it may be recalled that the interpretation of our previous results was made in terms of hydrogen-ion concentrations derived from ionisation constants in the case of weak acids, from conductivity data in the case of strong acids, and from the application of the mass law and the principle of isohydry in the case of acid–salt mixtures.

The method used for acid–salt mixtures is admittedly open to criticism, and for this reason we directed our attention to mixtures of acetic acid and sodium acetate, for which electrometric hydrogen-ion concentrations are afforded by Walpole's careful measurements of hydrogen potential (J., 1914, **105**, 2501). The mixtures actually used by Walpole form two series: (1) $(0{\cdot}2 - x)N\text{-}CH_3{\cdot}CO_2H + xN\text{-}CH_3{\cdot}CO_2Na$; (2) $(0{\cdot}2 - x)N\text{-}(CH_3{\cdot}CO_2H + NaCl) + xN\text{-}CH_3{\cdot}CO_2Na$. In the former, the total acetate concentration is constant, whilst the latter series is distinguished by constancy of both total acetate and total salt concentration. The combination of two such series of mixtures in catalytic experiments appeared to offer the possibility of eliminating the disturbing effects of the varying interionic forces which are necessarily associated with variations in salt concentration. Actually, however, the mutual relations exhibited by the velocity data for mixtures belonging to these two series are by no means of a simple kind, and such mixtures are not nearly so satisfactory for the elucidation of the relevant factors as are those series of mixtures in which the concentration of the acid is kept constant.

Walpole's measurements are, nevertheless, of considerable significance in connexion with our experiments on acetic acid mixtures. They have shown that the electrometric hydrogen-ion concentrations of solutions belonging to the above series lead to values for the ionisation constant, $K_a = [H]^+[A]^-/[HA]$, which are not only independent of the salt/acid ratio over a very wide range, but are also in good agreement with the value of K_a given by the conductivity of solutions of the pure acid. In other words, it

seems probable that there is very little difference between the thermodynamic concentrations of the ionised acid in the presence of the salt and the concentrations indicated by conductivity data for solutions of the free acid. This relative freedom from the disturbing influence of ionic environment for mixtures of acetic acid and sodium acetate is, however, not peculiar to the ionised acid, for, by measurements of the partial pressure of acetic acid in aqueous solutions of various salts, McBain and Coleman (J., 1914, **105**, 1517) have shown that the changes of pressure produced by the addition of sodium acetate are very small compared with those produced, for instance, by sodium chloride.

The above facts are adduced with the object of emphasising the circumstance that the conditions attaching to the use of acetic acid–sodium acetate mixtures in the investigation of the problem of catalysis seemed to be particularly favourable, in that the volume concentrations of the hydrogen ion and of the undissociated acid are probably very little different from the thermodynamic concentrations. For the corresponding series of mixtures, in which the acetic acid is replaced by monochloroacetic acid, there is no evidence which bears on this question.

Most of the experiments we describe in this paper have reference to acid–salt mixtures in which the concentration of the acid is kept constant, whilst that of the salt is varied. For such mixtures no hydrogen potentials are available, and we have therefore undertaken these measurements with a view to the determination of the hydrogen-ion concentration of the solutions employed.

Purification of Materials.—Acetone was obtained by decomposition of the sodium iodide compound and fractionation of the product; b. p. 56·2—56·3°.

Acetic acid. The impurities in acetic acid which react with iodine were removed by the permanganate method (Lowry and Bousfield, J., 1911, **99**, 1432). The product, after fractionation, was again treated with permanganate and the process repeated three or four times; m. p. 16·25°.

Monochloroacetic acid. The fraction of the commercial acid distilling at 185—186° (uncorr.) was crystallised from benzene; m. p. 60·8—60·9°.

Sodium acetate. The salt was recrystallised four times from conductivity water.

Sodium monochloroacetate. Solution prepared by neutralisation of the acid.

Electrometric Measurements.

The *E.M.F.* of cells of the type

$$H_2|HA + NaA|Sat.KCl|0{\cdot}1N\text{-}KCl, Hg_2Cl_2|Hg$$

was measured in the usual manner. The hydrogen used was passed through alkaline permanganate, saturated mercuric chloride, alkaline pyrogallol, and the solution under investigation before it entered the hydrogen vessel. The results obtained are in Tables I and II, which give the hydrogen-ion concentrations, expressed in terms of p_H, derived from the equation $p_H = (E - 0{\cdot}338)/0{\cdot}0001985T$.

TABLE I.

0·1*N*-$CH_3{\cdot}CO_2H$ + *x*N-CH_3CO_2Na.				0·2*N*-$CH_3{\cdot}CO_2H$ + *x*N-$CH_3{\cdot}CO_2Na$.		
x.	*E*.	*T*.	p_H.	*E*.	*T*.	p_H.
0	0·502	288°	2·87	0·492	288°	2·69
0·0048	0·534	287	3·44	0·518	288	3·15
0·0096	0·546	288	3·64	0·530	284	3·41
0·0192	0·562	286	3·94	0·544	285	3·64
0·0480	0·588	293	4·30	0·566	286	4·02
0·0961	0·604	291	4·61	0·583	287	4·30
0·1922	0·619	291	4·87	0·599	288	4·56
0·480	0·642	289	5·30	0·623	288	4·98
0·961	0·660	289	5·61	0·642	289	5·30

TABLE II.

0·05*N*-$CH_2Cl{\cdot}CO_2H$ + *x*N-$CH_2Cl{\cdot}CO_2Na$.				0·1*N*-$CH_2Cl{\cdot}CO_2H$ + *x*N-$CH_2Cl{\cdot}CO_2Na$.		
x.	*E*.	*T*.	p_H.	*E*.	*T*.	p_H.
0	0·453	286°	2·03	0·446	288°	1·89
0·01	0·466	287	2·25	0·455	291	2·03
0·02	0·475	289	2·39	0·460	287	2·14
0·04	0·484	287	2·56	0·469	288	2·29
0·10	0·505	284	2·96	0·488	289	2·62
0·20	0·517	285	3·16	0·502	287	2·88
0·50	0·530	286	3·38	0·515	286	3·12

The electrometric values of p_H recorded in the foregoing tables have been compared with the values calculated from the mass-law expression for the dissociation of the acid, *viz.*,

$$K_a = [H]^+(\alpha C' + [H]^+)/(C - [H]^+),$$

in which K_a for acetic acid $= 1{\cdot}85 \times 10^{-5}$, for chloroacetic acid in 0·05*N*-solutions $= 0{\cdot}16 \times 10^{-2}$, and in 0·1*N*-solutions $= 0{\cdot}17 \times 10^{-2}$; C and C' are the concentrations of the acid and salt, respectively, and α is the coefficient * for the salt given by the conductivity ratio at the ionic concentration $\alpha C'$. In actual practice, an approximate estimation of $[H]^+$ was made and the value of p_H calculated from the corresponding logarithmic formula

$$p_H = \log 1/K_a + \log (\alpha C' + [H]^+)/(C - [H]^+).$$

In the case of the acetic acid–sodium acetate mixtures, the calculated

* The values of this coefficient correspond closely with the thermodynamic degrees of dissociation recorded by Lewis and Randall for a uni-univalent electrolyte.

values of p_H agree very closely with those derived from the hydrogen-potential measurements. The difference between them is less than 0·03 when the salt concentration is not greater than 0·2N. For the two most concentrated solutions, the divergence is greater, but this is of no consequence in so far as the velocity measurements are concerned, for in these concentrated salt solutions (0·5 and 1·0N) the hydrogen-ion concentration is so small that its catalytic effect is negligible. Generally speaking, the results justify the belief that for acetic acid mixtures, hydrogen-ion concentrations of the desired degree of accuracy may be obtained either from hydrogen-potential measurements or by the use of the mass-law expression.

For mixtures of chloroacetic acid and sodium chloroacetate, the agreement between the electrometric and mass-law values of p_H is not nearly so good as for the acetate mixtures. The curves obtained by plotting the two series of p_H values against the logarithm of the salt concentration (x) are approximately linear when x is not too small. For salt concentrations less than 0·2N, the difference between the two curves does not exceed about 0·1 unit on the p_H scale. Since, however, differences in p_H are a measure of relative differences in hydrogen-ion concentration, the magnitude of the divergence between the two sets of values may be more appropriately shown by a comparison of the degrees of ionisation. In Table III, the percentage degrees of ionisation of the acid corresponding with the hydrogen-potential measurements are recorded under α_1, whilst those derived from the mass-law are given under α_2.

TABLE III.

Ionisation of Chloroacetic Acid in Admixture with Sodium Chloroacetate (xN).

	x	0·01	0·02	0·03	0·05	0·1	0·2	0·5
0·05N-Acid	α_1	11·25	8·15	6·60	4·60	2·45	1·32	0·59
	α_2	10·35	7·10	5·35	3·60	1·95	1·03	0·46
0·10N-Acid	α_1	9·35	7·25	5·75	4·15	2·50	1·41	0·69
	α_2	8·85	6·65	5·25	3·65	2·02	1·09	0·50

For the purpose to which the data in question are to be applied the differences between the two sets of ionisation values are not of serious moment. The series of electrometric values serves to confirm the general accuracy of the mass-law values, but if a distinction is to be made, we prefer the latter on the ground that the hydrogen-potential measurements possibly involve a diffusion potential of unknown magnitude.

Measurements of Reaction Velocity.

The procedure followed in the determination of the initial velocity of the reaction between acetone and iodine was essentially the same

as that described by Dawson and Powis (*loc. cit.*). The concentration of the acetone was throughout 20 c.c. per litre (0·272*M*), the iodine about 0·005*M*, and the temperature 25°.

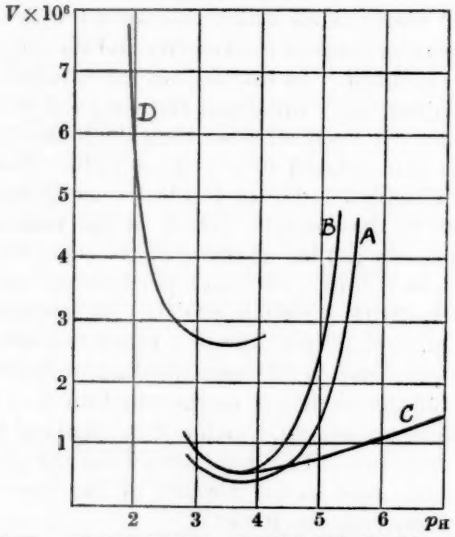
The general character of the results obtained may be described by reference to the data for catalysing mixtures represented by the general formula $aN\text{-}CH_3\cdot CO_2H + xN\text{-}CH_3\cdot CO_2Na$, where a is constant and x variable. As the hydrogen-ion concentration is reduced by continual increase in the proportion of sodium salt, the initial velocity falls, rapidly at first, then less and less quickly, passes through a minimum and then increases continuously, until, in presence of 1·0*N*-sodium acetate, the velocity is approximately five times as great as in the absence of salt. For salt concentrations which are well above those which correspond with the minimum velocity, the relation between the velocity and the salt concentration is almost exactly linear. In this region, the catalytic effect of the hydrogen ion is negligibly small and the observed reaction velocity must be attributed to agencies other than the hydrogen ion. If the straight line is extrapolated to $x = 0$, catalytic effects due to the added salt are eliminated and the residual velocity should therefore be attributable to the catalytic action of the undissociated acid. The residual velocity (v_r) for mixtures of the series $0{\cdot}1N\text{-}CH_3\cdot CO_2H + xN\text{-}CH_3\cdot CO_2Na$ is $0{\cdot}15 \times 10^{-6}$ mol. per litre per minute; for the series $0{\cdot}2N\text{-}CH_3\cdot CO_2H + xN\text{-}CH_3\cdot CO_2Na$, the residual velocity is $0{\cdot}30 \times 10^{-6}$ mol. per litre per minute. In other words, the residual velocity is proportional to the concentration of the acetic acid (a) and the value of the coefficient in the equation $v_r = k \,.\, a$ is $1{\cdot}5 \times 10^{-6}$ mol. per litre per minute, which is thus identical with the value of k_m for the undissociated acid obtained from the previous experiments with acetic acid in the absence of the corresponding salt (Dawson and Powis, *loc. cit.*, p. 2143).

When the data for the experiments with mixtures of chloroacetic acid and sodium chloroacetate corresponding with the formula $0{\cdot}1N\text{-}CH_2Cl\cdot CO_2H + xN\text{-}CH_2Cl\cdot CO_2Na$ are examined in the same way, exactly similar relations are found. The residual velocity obtained by extrapolation is $2{\cdot}4 \times 10^{-6}$, which gives for k_m the value 24×10^{-6}. This again is identical, within the limits of error, with the value $k_m = 24{\cdot}5 \times 10^{-6}$ derived by Dawson and Powis for the coefficient representing the catalytic activity of undissociated monochloroacetic acid from observations on the catalysing power of the free acid at a series of different concentrations. In order to illustrate diagrammatically the nature of our results in such a way as to include not only the entire range of salt concentrations, but also the results which have been obtained for mixtures in which the acid concentrations, as well as those in which the total acetate

concentration was constant, it is advantageous to plot the observed velocity against p_H. Such curves are shown in the diagram. They show that the reaction velocity is smallest in the neighbourhood of $p_H = 3{\cdot}8$ when the reaction is catalysed by the acetic acid mixtures and at about $p_H = 3{\cdot}5$ when catalysed by the chloroacetic acid mixtures.

The catalytic activity of the undissociated acid has thus been demonstrated by two independent methods. In the first of these, the evidence is based on velocity data for solutions which contain no salt and for which the hydrogen-ion concentration is derived

FIG. 1.



A. 0·1*N*-$CH_3{\cdot}CO_2H + x$*N*-$CH_3{\cdot}CO_2Na$. *B*. 0·2*N*-$CH_3{\cdot}CO_2H + x$*N*-$CH_3{\cdot}CO_2Na$.
C. (0·2-*x*)*N*-$CH_3{\cdot}CO_2H + x$*N*-$CH_3{\cdot}CO_2Na$.
D. 0·1*N*-$CH_2Cl{\cdot}CO_2H + x$*N*-$CH_2Cl{\cdot}CO_2Na$.

from the electrical conductance. The second method does not involve any knowledge of the degree of ionisation of the acid. It is merely assumed that the ionisation of the weak acid is reduced to a negligible value by the addition of a sufficient quantity of the corresponding salt and that the velocity, over and above that which is attributable to the added salt, represents the effect which is due to the undissociated acid. The identity of the values of k_m obtained by these independent methods affords a very remarkable confirmation of the view that catalytic activity must be ascribed to the acid in its undissociated form.

At higher salt concentrations, as already pointed out, the con-

nexion between the observed reaction velocity, v, and the concentration (x) of the added salt may be accurately represented by the linear formula

$$v = v_r + k'x$$

in which $v_r = k_m \,.\, a$ represents the residual velocity and k' is a constant which measures the catalytic activity of the salt. The magnitude of k', given by the slope of the linear portions of the velocity curves, depends to a large extent on the nature of the acid anion. It is very much larger for the acetate ($k' = 4{\cdot}5 \times 10^{-6}$) than for the chloroacetate ($k' = 0{\cdot}12 \times 10^{-6}$).

If we accept the view that the salts are completely ionised, it would appear that the active catalytic agents concerned are the respective anions, and that the reaction which is characterised by the coefficient k' is closely similar to the catalysed decomposition of nitroamide recently studied by Brönsted and Pedersen (*Z. physikal. Chem.*, 1924, **108**, 185). For both reactions, the catalytic activity of the acid ion increases as the dissociation constant of the corresponding acid diminishes. Such a relation would lead us to expect that the hydroxyl ion would be a very active catalyst for the acetone–iodine reaction, and there is direct evidence to support this view.

In conformity with the actual development of the theoretical interpretation we shall, however, confine our attention to experimental conditions, in which the catalytic effect of the hydroxyl ion, by reason of its very low concentration, may be left out of account. With this proviso, the results we have obtained lead to the conclusion that the observed velocity of reaction represents the sum of the effects due respectively to the catalytic action of the hydrogen ion, the undissociated acid, and the acid ion.

The equation for the observed velocity may therefore be written :

$$\begin{aligned} v &= v_h + v_m + v_a \\ &= k_h[\mathrm{H}]^+ + k_m[\mathrm{HA}] + k_a[\mathrm{A}]^- \,. \quad . \quad (1) \end{aligned}$$

in which k_h, k_m, and k_a represent respectively the catalytic coefficients for the hydrogen ion, the acid molecule, and the acid ion. The relative importance of the three partial velocities depends on the concentrations of the respective catalytic agents and on the relative magnitudes of the corresponding coefficients. By the continued addition of salt to a given solution of the free acid, it may be possible to realise successively conditions in which the dominant catalyst is either the hydrogen ion, the undissociated acid, or the acid anion.

In the case of acetic acid, for which the coefficients ($\times 10^6$) have the values $k_h = 442$, $k_m = 1{\cdot}5$, and $k_a = 4{\cdot}5$, this has been actually accomplished, as may be seen from an inspection of Table IV, in

which the relevant data for mixtures $0{\cdot}1N$-$CH_3{\cdot}CO_2H + xN$-$CH_3{\cdot}CO_2Na$ are set out in detail. Col. 1 gives the salt concentration; col. 2 the concentration of the hydrogen ion $[H]^+$, from which the concentrations of the undissociated acid, $[HA] = 0{\cdot}1 - [H]^+$, and of the acid ion, $[A]^- = x + [H]^+$, may be derived; cols. 3, 4, and 5, the partial velocities v_h, v_m, and v_a due to the hydrogen ion, undissociated acid, and acid ion, respectively; col. 6 gives the total velocity calculated from equation (1), and col. 7 gives the velocity actually observed.†

TABLE IV.

Catalyst: $0{\cdot}1N$-$CH_3{\cdot}CO_2H + xN$-$CH_3{\cdot}CO_2Na$.

x.	$[H]^+ . 10^4$.	$v_h . 10^6$.	$v_m . 10^6$.	$v_a . 10^6$.	$v_{cal.} . 10^6$.	$v_{obs.} . 10^6$.
0	13·5	0·596	0·148	0·006	0·75	0·75
0·005	3·67	0·162	0·149	0·024	0·335	0·36
0·010	2·00	0·088	0·150	0·046	0·285	0·31
0·020	1·06	0·047	0·150	0·090	0·29	0·31
0·025	0·86	0·038	0·150	0·113	0·30	0·32
0·050	0·45	0·020	0·150	0·225	0·395	0·405
0·1	0·24	0·010	0·150	0·450	0·61	0·60
0·2	0·13	0·006	0·150	0·900	1·055	1·04
0·3	0·09	0·004	0·150	1·350	1·505	1·51
0·4*	0·07	0·003	0·150	1·800	1·95	1·95
0·5*	0·06	0·002	0·150	2·250	2·40	2·45
1·0*	0·03	0·001	0·150	4·500	4·65	4·6

Examination of the table shows that there is close agreement between the calculated and observed reaction velocities over the entire range of acid–salt mixtures. At low salt concentrations, the chief catalyst is the hydrogen ion, but between 0·01 and $0{\cdot}025N$ concentrations the largest effect is produced by the undissociated acid, and at still higher concentrations the dominant part is played by the acetate ion.

The results for a similar series of mixtures with acid of $0{\cdot}2N$ concentration are given in Table V in abbreviated form, the partial velocities being omitted. The agreement between the calculated and observed velocities is very similar to that in the previous table.

TABLE V.

$0{\cdot}2N$-$CH_3{\cdot}CO_2H + xN$-$CH_3{\cdot}CO_2Na$.

x	0	0·004	0·010	0·020	0·050	0·10	0·20	1·0*
$[H]^+ . 10^4$ ...	19·2	8·13	3·92	2·10	0·88	0·47	0·25	0·07
$v_{cal.} . 10^6$ ...	1·15	0·68	0·52	0·485	0·565	0·77	1·21	4·80
$v_{obs.} . 10^6$ ...	1·16	0·65	0·50	0·46	0·545	0·775	1·27	4·8

Attention may now be directed to the results of experiments

† The difference between the calculated values given by equation (1) and the more general equation (2) (considered later) increases from $0{\cdot}01 \times 10^{-6}$ for $x = 0{\cdot}2$ to $0{\cdot}05 \times 10^{-6}$ for $x = 1{\cdot}0$. For the sake of simplicity we have considered it preferable to use the original simple form of our equation for this type of acid–salt mixture.

with catalytic mixtures corresponding with the series $(0{\cdot}2 - x)N\text{-}CH_3{\cdot}CO_2H + xN\text{-}CH_3{\cdot}CO_2Na$, in which the total acetate concentration is constant. For the mixtures in this series, the hydrogen-ion concentration is that given by Walpole's hydrogen-potential measurements. In the case of the free acid, the value has been derived from $K_a = 1{\cdot}85 \times 10^{-5}$.

As the ratio of salt to acid in this series of mixtures increases, the values of $[H]^+$ and $[HA]$ diminish continuously and equation (1) would suggest that the reaction velocity should eventually rise to a maximum limiting value given by $v = k_a[A]^- = 4{\cdot}5 \times 10^{-6} \times 0{\cdot}2 = 0{\cdot}9 \times 10^{-6}$. This, however, is not the case. For the last member of the series ($0{\cdot}002N\text{-}CH_3{\cdot}CO_2H + 0{\cdot}198N\text{-}CH_3{\cdot}CO_2Na$) the observed value exceeds this limit by 40%. Moreover, there is a systematic divergence between the observed and calculated velocities for solutions of low acid concentrations, in that the difference between them increases continuously as the concentration of the acid is reduced.

For the solutions in question, the hydrogen-ion concentration is very small, and since the product $[H]^+ . [OH]^-$ is constant, it would seem that conditions have been reached in which the concentration of the hydroxyl ion is such that its catalytic effect must be taken into account. If the velocities for the mixtures containing 0·01, 0·005, and $0{\cdot}002N$-acid are calculated from equation (1) and subtracted from the observed velocities, the differences should represent the partial velocities due to the hydroxyl ion in the three experiments concerned. From these numbers the catalytic coefficient for the hydroxyl ion may be derived from the equation $v_{OH} = k_{OH} . [OH]^- = k_{OH} . K_w/[H]^+$, in which K_w is the ionisation constant for water $= 1 \times 10^{-14}$. The numbers obtained in this way for the three acid–salt mixtures in question are respectively 9·0, 11·5 and 9·2, giving as a mean $k_{OH} = 10$.

The concordance between the separate values is as good as could possibly be expected and is obviously quite consistent with the view that such mixtures provide conditions in which the hydroxyl ion takes a measurable part in the catalysis of the reaction. In order to include the range of conditions which are afforded by mixtures in which the acid concentration is small and the ratio of salt to acid large, it is evident that equation (1) must be extended to include a term corresponding with the hydroxyl ion. The complete equation thus becomes

$$\begin{aligned} v &= v_h + v_m + v_a + v_{OH} \\ &= k_h[H]^+ + k_m[HA] + k_a[A]^- + k_{OH}[OH]^- \qquad (2), \end{aligned}$$

in which the coefficient k_{OH} is very much greater than any of the

other three. The ratio k_{OH}/k_h is given by $10/(442 \times 10^{-6})$ and, according to this, the catalytic activity of the hydroxyl ion is more than 20,000 times as great as that of the hydrogen ion.

Table VI affords a comparison of the velocities calculated from equation (2) with those actually observed. The arrangement is similar to that adopted in Table IV.

TABLE VI.

$(0{\cdot}2 - x)N\text{-}CH_3{\cdot}CO_2H + xN\text{-}CH_3{\cdot}CO_2Na.$

x.	$[H]^+ \times 10^4$.	$v_h \times 10^6$.	$v_m \times 10^6$.	$v_a \times 10^6$.	$v_{OH} \times 10^6$.	$v \times 10^6$ (calc.).	$v \times 10^6$ (obs.).
0	19·2	0·848	0·297	0·009	nil	1·15	1·16
0·015	2·51	0·110	0·278	0·069	nil	0·455	0·46
0·024	1·58	0·070	0·264	0·109	nil	0·445	0·44
0·036	1·00	0·044	0·246	0·162	nil	0·45	0·46
0·053	0·63	0·028	0·221	0·239	0·001	0·49	0·495
0·074	0·40	0·018	0·189	0·333	0·002	0·54	0·54
0·098	0·25	0·011	0·153	0·441	0·004	0·61	0·59
0·141	0·11	0·004	0·089	0·635	0·010	0·74	0·74
0·158	0·063	0·002	0·063	0·711	0·016	0·795	0·80
0·171	0·041	0·002	0·045	0·770	0·024	0·84	0·835
0·181	0·025	0·001	0·030	0·815	0·040	0·885	0·88
0·190*	0·013	nil	0·015	0·855	0·077	0·945	0·94
0·195*	0·0062	nil	0·008	0·878	0·160	1·045	1·07
0·198*	0·0025	nil	0·003	0·891	0·400	1·295	1·26

The agreement between the calculated and observed reaction velocities is clearly such as to warrant the conclusion that the catalysis of the reaction takes place in accordance with equation (2). In view of the relations $K_a = [H]^+[A]^-/[HA]$ and $K_w = [H]^+[OH]^-$, this equation may be written in the form

$$v = k_h[H]^+ + k_m \cdot [HA] + k_a \cdot K_a[HA]/[H]^+ + k_{OH} \cdot K_w/[H]^+ \quad (3),$$

in which the only variable parameters are the concentrations of hydrogen ions and of undissociated acid. Since the last two terms in equation (3) both involve the concentration of the hydrogen ion to the inverse first power, it is apparent that series of acid–salt mixtures, in which the concentration of the acid is kept constant, do not afford the appropriate conditions for distinguishing experimentally between the catalytic effects which are produced by the acid ion and the hydroxyl ion, respectively. This is exactly in accordance with our experience.

In reference to the very wide variation of the conditions under which the velocity of the reaction has been measured by the use of acetic acid–salt mixtures, it may be pointed out that the final products are not independent of the hydrogen-ion concentration of the solution. In those experiments in Tables IV, V, and VI which are distinguished by a star in the salt column (x*), it was observed that iodoform was formed. Although we do not propose to discuss here the mechanism of the reaction between acetone and iodine

apart from the catalytic effects which are associated with it, it may be stated that low values of hydrogen-ion concentration undoubtedly provide conditions which facilitate the progress of those reactions which succeed the slow reaction the velocity of which has been measured, and lead ultimately to the separation of iodoform. The disturbing effect of these after-reactions is, we believe, almost entirely eliminated by our experimental procedure, in which the initial velocity of the slow primary reaction is measured. For this reason, we do not propose to discuss here certain observations which have reference to the formation of iodoform as the final product of the reaction.

It should, however, be stated that the formation of hydriodic acid as a product associated with the primary reaction constitutes a factor which of necessity tends to complicate the determination of the initial velocity when the proportion of acid to salt becomes very small. This ratio is 1 : 100 in the last recorded experiment in Table VI, and although it may be possible to make measurements with solutions which contain a still smaller proportion of acid, it will be readily understood that such measurements would necessitate special precautions in the experimental conditions to ensure that the value of the ratio $[H]^+/[OH]^-$ is not unduly disturbed in the very earliest stage of the reaction by the hydriodic acid which is formed.

In Table VII are recorded the data for mixtures of monochloroacetic acid and sodium monochloroacetate. Some of these measurements were made by Dawson and Reiman, and for the observations at high salt-concentrations we are indebted to Mr. C. R. Hoskins. Since chloroacetic is a much stronger acid than acetic, there are no effects which are attributable to the hydroxyl ion. The velocities of reaction have been calculated from the equation

$$v = 442 \times 10^{-6}[H]^+ + 24 \times 10^{-6}[HA] + 0{\cdot}12 \times 10^{-6}[A]^-$$

TABLE VII.

	0·05*N*-$CH_2Cl{\cdot}CO_2H$ + *x*N-$CH_2Cl{\cdot}CO_2Na$.			0·1*N*-$CH_2Cl{\cdot}CO_2H$ + *x*N-$CH_2Cl{\cdot}CO_2Na$.		
x.	$[H]^+ \times 10^2$.	$v \times 10^6$ (calc.).	$v \times 10^6$ (obs.).	$[H]^+ \times 10^2$.	$v \times 10^6$ (calc.).	$v \times 10^6$ (obs.).
0	0·82	4·63	4·90	1·22	7·50	7·75
0·01	0·518	3·37	3·38	0·884	6·10	6·18
0·02	0·356	2·69	2·70	0·667	5·19	5·12
0·03	0·268	2·32	2·29	0·523	4·59	4·52
0·05	0·180	1·96	1·84	0·363	3·92	3·77
0·10	0·098	1·62	1·50	0·202	3·26	3·04
0·20	0·0515	1·44	1·34	0·109	2·88	2·64
0·50	0·021	1·35	1·35	0·045	2·65	2·65
0·896				0·023	2·60	2·53
1·57				0·015	2·63	2·64
2·13				0·010	2·70	2·69
3·20				0·008	2·82	2·80

in which, in accordance with the assumption of complete ionisation of the salt, $[A]^- = x + [H]^+$ where x is the stoicheiometric salt concentration. The values of $[H]^+$ are based on the mass-law formula with $K_a = 0{\cdot}16 \times 10^{-2}$ for the 0·05*N*-acid series, and $K_a = 0{\cdot}17 \times 10^{-2}$ for the 0·1*N*-acid series.

In regard to the variations in the effects of the three catalysts the chloroacetic acid mixtures are not quite so interesting as the acetic acid mixtures, but there can be little doubt that the relations involved are of the same kind.

By the detailed study of the catalytic properties of mixtures of a weak acid with its corresponding salt, it has thus been possible to show that catalytic effects must be attributed to the hydrogen ion, the acid molecule, and the acid ion. In the absence of salt, the relations will, of course, be the same, and the relative importance of the catalytic effects due to the ions and molecules respectively will depend on the concentration of the acid. By the addition of salt, the relative magnitudes of the effects can be altered within wider limits for the purpose of actual measurement and conditions may actually be realised in which either of them has the dominant rôle. When the acid is weak and the ratio of salt to acid becomes sufficiently great, a fourth catalytic effect, namely, that due to the hydroxyl ion, comes into play.

Of the molecular and ionic entities which are commonly supposed to be present in aqueous solutions of mixtures of acids and their salts, *viz.*, H^+, M^+, A^-, OH^-, HA, and H_2O, four have been found to act as catalysts in the acetone–iodine reaction. There is no evidence that the metallic cation has any measurable activity, but our experiments have not been specifically designed to detect any very small effect of this kind. We also see no reason for attributing activity to the water molecule. The fact that the activity of the undissociated acid falls rapidly as the tendency to ionise diminishes —for acetic acid it is only about $\frac{1}{15}$ as large as for monochloroacetic acid—would suggest that the activity of the water molecule is very small.

It is extremely probable that the relative magnitudes of the various catalytic coefficients will vary widely with the nature of the catalysed reaction. In this connexion it may be noted that in the reaction between monochloroacetone and iodine, which appears to be closely similar to the reaction we have studied, the catalytic coefficients for the hydrogen ion and the undissociated acetic acid are much smaller in comparison with the coefficient for the acetate ion than is the case for the acetone reaction. On the other hand, the measurements of Arrhenius (*Z. physikal. Chem.*, 1890, **5**, 1) on the inversion of sucrose would seem to show that the

catalytic activities of the undissociated acid and of the acetate ion are exceedingly small in comparison with that of the hydrogen ion.

The possibility of realising conditions in which, by adjustment of the acid–salt ratio, the chief catalytic effect is due to the hydrogen ion, the undissociated molecule, or the acid ion, depends on the dissociation constant of the acid and on the absolute concentration.

By the addition of sodium chloride or other catalytically inert salt to the catalysing mixture of acetic acid and sodium acetate, changes in the velocity of reaction are produced which depend on the composition of the mixture, *i.e.*, on the relative magnitudes of the effects which are attributable to the positive ion, the negative ion and the undissociated molecule respectively.

In conclusion, it may be noted that measurements of the velocity of the acetone reaction with strong acids as catalysts (compare Dawson and Crann, J., 1916, **109**, 1262) have been previously interpreted in a manner analogous to that adopted for the weak acids, the conductivity ratio λ/λ_∞ being used as a measure of the hydrogen-ion concentration. The experimental data suggested that the undissociated molecules of these strong acids are more active catalysts than the hydrogen ion ($k_m > k_h$). Accepting the view that such acids are completely ionised, the previous interpretation of the velocity data can no longer be maintained. It seems possible that the phenomena observed in the action of the strong acids may be due, not to effects which are directly comparable with those described here for the weaker acids, but to changes in the activity of the hydrogen ion which are attributable to changes in environment such as are responsible for the difference between thermodynamic and volume concentrations. So far as the catalytic experiments described in this paper are concerned, the question of distinguishing between the activity and the stoicheiometric concentration of the catalytically active agents does not appear to be of primary importance, although it is by no means suggested that such distinction can be always ignored.

In accordance with previous practice, the values of the velocity coefficients recorded in this paper refer to a concentration of 20 c.c. of acetone per litre. To express them in terms of 1 g.-mol. of acetone per litre, the numbers in question must be multiplied by $1/0{\cdot}272 = 3{\cdot}67$.

General Conclusions.

The phenomena observed in the catalysis of a reaction in aqueous solutions of weak acids and mixtures of these with the corresponding salts lead to the conclusion that catalytic effects are attributable to the hydrogen ion, the undissociated acid, the acid ion, and the hydroxyl ion.

The general equation, in terms of which the observed reaction velocities can be expressed, is of the form :

$$v = k_h[\mathrm{H}]^+ + k_m[\mathrm{HA}] + k_a[\mathrm{A}]^- + k_{\mathrm{OH}}[\mathrm{OH}]^-$$

in which k_h, k_m, k_a and k_{OH} are the respective velocity coefficients.

By suitable adjustment of the proportions in which acetic acid is mixed with sodium acetate, any one of the four catalysts may be made to play the dominant rôle as catalytic agent. Both for acetic and monochloroacetic acids, the values obtained for the catalytic coefficient of the undissociated acid by two entirely independent methods are identical within the limits of experimental error.

The relative values of the coefficients k_h, k_a, and k_m vary widely with the strength of the acid as measured by its dissociation constant.

In view of the composite nature of the catalytic phenomena, the effects produced by the addition of a foreign, catalytically inert, salt will depend on the nature of the dominant catalyst and such effects will not in general be directly comparable with one another.

The electrometric values of the hydrogen-ion concentration of solutions containing mixtures of chloroacetic acid and its sodium salt are in satisfactory agreement with those derived from the mass law. The agreement is, however, not so close as that shown by mixtures of acetic acid and sodium acetate.

THE UNIVERSITY, LEEDS. [*Received, June 10th*, 1926.]

CCCIII.—*Imino-aryl Ethers. Part IV. Reversible Migration of an Aryl Group.*

By ARTHUR WILLIAM CHAPMAN.

IN Part III of this series (J., 1925, **127**, 1992) it was shown that *N*-phenylbenziminophenyl ether (I) may be converted into benzoyldiphenylamine (II) on heating, and that this change was unimolecular, complete and without by-products :

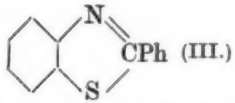
$$\text{(I.)}\ \mathrm{PhO{\cdot}CPh{:}NPh} \xrightarrow{\text{heat}} \mathrm{O{:}CPh{\cdot}NPh_2}\ \text{(II.)}$$

As the behaviour of the corresponding imino-thioether seemed likely to throw additional light on this isomeric change, N-*phenylbenziminophenyl thioether* (VI) and N-p-*tolylbenzimino*-p-*tolyl thioether* were prepared.

When *N*-phenylbenziminophenyl thioether (VI) was heated for 2 hours at 280—290°, a treatment which is sufficient to cause complete isomeric change of the *O*-ether, only a small amount of thio-

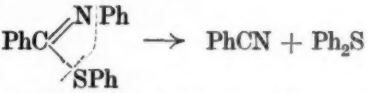
benzoyldiphenylamine (VII) was produced, most of the material being unchanged. The migration of the phenyl group from sulphur to nitrogen was therefore much more sluggish than that from oxygen to nitrogen in an otherwise similar case. Thiobenzoyldiphenylamine under similar conditions suffered practically no change.

At higher temperatures, especially at 320° and above, decomposition of the imino-thioether took place, the products isolated being diphenyl sulphide, benzonitrile, thiophenol, and 1-phenylbenzthiazole (III).

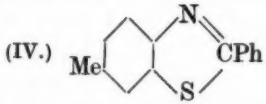


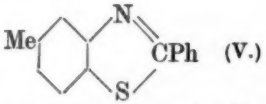
(III.)

The production of thiophenol and 1-phenylbenzthiazole is not easily explicable, but the diphenyl sulphide and benzonitrile, isolated in yields of up to 29%, can be regarded as derived by the disruption of the imino-thioether molecule, thus :



When *N*-*p*-tolylbenzimino-*p*-tolyl thioether was heated under similar conditions, 1-phenyl-5-methylbenzthiazole (IV) was produced and not 1-phenyl-4-methylbenzthiazole (V), so that the formation of the thiazole from the imino-thioether is effected, either by elimination of the group attached to the sulphur atom, or by previous migration of this group to the nitrogen atom.





The yields of 1-phenylbenzthiazole obtained by heating *N*-phenylbenziminophenyl thioether and thiobenzoyldiphenylamine, respectively, under identical conditions, were, however, not sufficiently different to enable a decision between these two views to be reached.

Thiobenzoyldiphenylamine, at 320° and above, yielded the same decomposition products as the imino-thioether in closely similar yields. It is not easy to see how diphenyl sulphide and benzonitrile and also thiophenol could be formed directly from a substance of the structure of thiobenzoyldiphenylamine, but the explanation at once becomes simple if it is assumed that *N*-phenylbenziminophenyl thioether is an intermediate product in the decomposition :

$$\underset{\text{PhSH},C_{13}H_9NS}{\overset{Ph_2S,PhCN,}{}} \longleftarrow \underset{\text{(VI.)}}{SPh\cdot CPh{:}NPh} \rightleftharpoons \underset{\text{(VII.)}}{S{:}CPh\cdot NPh_2}.$$

The conclusion therefore seems inevitable, that, although the high temperature at which the isomeric change takes place renders the attainment of an actual equilibrium impossible, the reaction here investigated is reversible, the phenyl group migrating between sulphur and nitrogen in either direction.

EXPERIMENTAL.

N-*Phenylbenziminophenyl thioether* was prepared from benzanilide-iminochloride and thiophenol by the method used for preparing *N*-phenylbenzimino-*m*-hydroxyphenyl ether (J., 1922, **121**, 1679), all operations involving alkaline solutions of thiophenol being conducted in an atmosphere of nitrogen. It crystallised from alcohol in stout yellow prisms, m. p. 58° (Found: N, 4·98. $C_{19}H_{15}NS$ requires N, 4·84%), and was hydrolysed by 50% sulphuric acid to aniline and phenyl thiolbenzoate (m. p. 56—57°, not depressing the m. p. of an authentic specimen).

N-p-*Tolylbenzimino*-p-*tolyl thioether*, prepared similarly from benz-*p*-toluidideiminochloride and *p*-thiocresol, crystallised from alcohol in yellow prisms, m. p. 50° (Found: N, 4·64. $C_{21}H_{19}NS$ requires N, 4·42%). On hydrolysis by 50% sulphuric acid, it furnished *p*-toluidine (m. p. 43—44°) and *p*-tolyl thiolbenzoate (m. p. 76°), both identified by direct comparison with authentic specimens.

Incidentally, *thiobenzoyldi*-p-*tolylamine* was prepared by heating a finely powdered mixture of benzoyldi-*p*-tolylamine with half its weight of phosphorus pentasulphide in a boiling brine-bath. After treatment with sodium hydroxide to remove unchanged phosphorus pentasulphide and repeated crystallisation from alcohol, in which it was very sparingly soluble, it yielded orange crystals, m. p. 189—190° (Found: N, 4·64. $C_{21}H_{19}NS$ requires N, 4·42%).

Comparative Heating of N-*Phenylbenziminophenyl Thioether and Thiobenzoyldiphenylamine.*—5 G. of material were used for each experiment. After the heating, the product was extracted with ether (30—40 c.c.) and any insoluble matter filtered off. This always consisted of unchanged thiobenzoyldiphenylamine. The ethereal extract was saturated with hydrogen chloride and the insoluble hydrochlorides separated. The solution was washed with sodium hydroxide to remove acid and thiophenol, dried and evaporated, and any residue of thiobenzoyldiphenylamine was crystallised from alcohol. The precipitated hydrochlorides were warmed with concentrated hydrochloric acid to convert the imino-thioether into phenyl thiolbenzoate and dissolve the 1-phenyl-benzthiazole, which was then recovered by pouring the acid solution into water. Both products were crystallised from alcohol.

The 1-phenylbenzthiazole (m. p. 114°) was identified by analysis

(Found: N, 6·66. $C_{13}H_9NS$ requires N, 6·63%) and by direct comparison with an authentic specimen.

N-*p*-tolylbenzimino-*p*-tolyl thioether, heated at 320° for 6 hours, yielded 1-phenyl-5-methylbenzthiazole (needles, m. p. 120—121°, not depressing the m. p. of a specimen prepared by the oxidation of thiobenz-*p*-toluidide, compare *Ber.*, 1886, **19**, 1068). Only small yields were obtained, and it was found that the substance readily chars under these conditions, whilst 1-phenylbenzthiazole is quite stable.

Identification of the Decomposition Products of N-*Phenylbenziminophenyl Thioether and of Thiobenzoyldiphenylamine.*—The substance under examination (20 g.), contained in a Claisen flask, was gradually heated in a very slow current of carbon dioxide, the volatile decomposition products being collected in a freezing mixture. Distillation commenced at about 330—340° and this temperature was maintained until distillation ceased (1—2 hours). The distillate was a yellowish liquid with an odour of thiophenol and contained some crystals of 1-phenylbenzthiazole. Redistillation gave two main fractions, b. p.'s 160—210° and 280—310°, respectively. No material of b. p. lower than 160° was isolated. The lower-boiling fraction consisted of thiophenol and benzonitrile. The thiophenol was identified by its odour, solubility in sodium hydroxide, and conversion by benzoyl chloride into phenyl thiolbenzoate (m. p. 57—58°, not depressing the m. p. of an authentic specimen). The benzonitrile was identified, after separation from the thiophenol, by the formation of a brown, crystalline compound with hydriodic acid, and by conversion with potassium hydroxide into ammonia and benzoic acid (m. p. 119—121°, not depressing the m. p. of an authentic specimen). The fraction boiling at 280—310° consisted of diphenyl sulphide, identified by oxidation with potassium permanganate to diphenylsulphone (m. p. 124—125°, not depressing the m. p. of an authentic specimen), and with concentrated nitric acid to diphenylsulphone and its di- and tetra-nitro-derivatives (m. p.'s 194—195° and 240°, respectively).

The residue in the decomposition flask was repeatedly extracted with boiling concentrated hydrochloric acid, and the 1-phenylbenzthiazole recovered by pouring the extracts into water. A small amount of dark-coloured tarry matter remained undissolved in the acid.

The yields of decomposition products were the same from both the imino-thioether and the thiobenzoyldiphenylamine. In a number of experiments, 10—13% of the calculated amount of thiophenol was isolated as phenyl thiolbenzoate, 16—29% as diphenyl sulphide, and 35—40% as 1-phenylbenzthiazole.

The author wishes to express his indebtedness to the Chemical Society for a grant which has defrayed part of the expenses of this investigation.

THE UNIVERSITY, SHEFFIELD. [*Received, July 13th*, 1926.]

CCCIV.—*Studies in Adsorption by an Optical Method. Fixation of Methylene-blue by Yeast-phospho-protein Sol within the Disperse Phase.*

By RASSA RIWLIN.

IN a previous paper on this subject (this vol., p. 102), Fodor and Riwlin showed that, working with sols of such proteins as casein, natural white of egg, purified albumin and gelatin, no difference was detectable spectrophotometrically between simple solutions of methylene-blue and solutions of this dye containing also any of these proteins. Our further researches on phospho-protein sol derived from yeast macerates have led to positive results.

The yeast phospho-protein was prepared by the method of Fodor (*Fermentforsch.*, 1921, **4**, 209), and contained 15·69% N and 5·95% S. It was insoluble in water, but readily formed a milky, colloidal suspension which wandered to the anode with the cataphoretic fall of potential. For its preparation from macerates of yeast, the fluid was diluted with water as required and fractionally precipitated with dilute hydrochloric acid.

The different fractions, after being thoroughly washed and dried, gave products which proved to be of the same composition on analysis but which, before drying (*i.e.*, in the freshly-precipitated condition), showed differing colloidal properties. The first fractions when rubbed with water gave a suspension—a stable, milky sol which kept as such for many days without sedimentation occurring. The fractions obtained with the more concentrated acid began to show sedimentation very soon.

The stable sols serve very well for adsorption experiments, particularly because of the fact that they contain slightly solvatised particles, which are clearly detectable ultra-microscopically and can be salted out. No other albuminous substance can be converted into ultra-visible sols in such a simple manner as can yeast-phospho-protein.

We determined by the spectrophotometric method previously described, the light-absorption of the following three mixtures:

1. Yeast-phospho-protein sol + water (transmissive power = a).

2. Yeast-phospho-protein sol + methylene-blue (transmissive power = b).

3. Methylene-blue + water (transmissive power = c).

When, in the case of the second mixture, no methylene-blue is withdrawn from the solution (as a result of adsorption by the phospho-protein particles), the transmissive power (b) is calculable from that of the two other solutions (a and c), *i.e.*, $b = ac$.

In all our determinations on phospho-protein it was found, however, that $b > ac$. This indicates that the mixture of methylene-blue and phospho-protein sol is more permeable to light than would be expected from the turbidity of the two separate solutions.

FIG. 1.

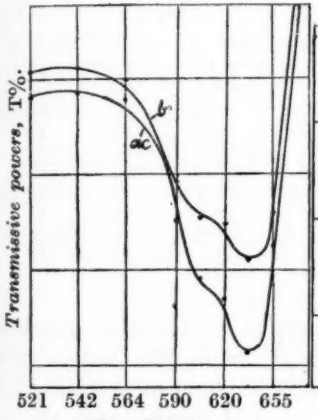
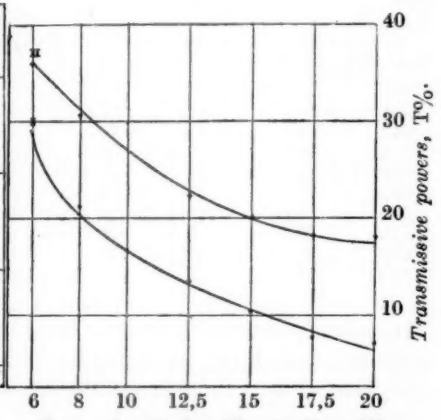


FIG. 2.



I = ac *and* II = b *for mixtures of methylene-blue + phospho-protein sol.*

Consequently, methylene-blue has disappeared from the solution, having accumulated on the surface of the phospho-protein particles.

From the fact that the transmission curve (Fig. 1) obtained from the calculated values of ac has the same form as that obtained from the values (b) actually found, it follows that we are dealing here with a non-chemical adsorption phenomenon. Moreover, the minima of the two curves occur at exactly the same wave-length. These facts, according to our previous work, indicate that we are dealing with true lyosorption.

From a very large number of observations, we quote here only one series which concerns mixtures of yeast-phospho-protein sol with increasing quantities of methylene-blue (Table I).

TABLE I.

Transmissive powers of mixtures of methylene-blue and phospho-protein sol.

% Conc. of methylene-blue.		6×10^{-4}.		8×10^{-4}.		10×10^{-4}.		$12{\cdot}5 \times 10^{-4}$.	
$\lambda(\mu\mu)$.	*a*.	*ac*.	*b*.	*ac*.	*b*.	*ac*.	*b*.	*ac*.	*b*.
521	50	47·5	52·5	47·5	50	45	46·5	45	45
542	54	49	51	48	50·5	46	46·5	43·5	45
564	59·5	49·5	50	47·5	49·5	41·5	42	40·5	37
590	64	39·5	45	35	39	28·5	34	25	27
604	65	34	39·5	29	35	23	32	19·5	25
620	68·5	31	37	26·5	34·5	20·5	30	17	24
637	70	29	36	21	30·5	16·5	27	13·5	22
655	70	29·5	40	27	35	21	30·5	18	25
674	70	59·5	60	56	57	52·5	50		

% Conc. of methylene-blue.		15×10^{-4}.		$17{\cdot}5 \times 10^{-4}$.		20×10^{-4}.	
$\lambda(\mu\mu)$.	*a*.	*ac*.	*b*.	*ac*.	*b*.	*ac*.	*b*.
521	50	43	45	41·5	44·5	38	41·5
542	54	43	43	40·5	42·5	38	40·5
564	59·5	35·5	36·5	33	35	30	33
590	64	19	27·5	16	25	13	19·5
604	65	15	25	12·5	20·5	9·5	18·5
620	68·5	13·5	22	10	19	9	18
637	70	10·5	20	7·5	18·5	7	18
655	70	17·5	24·5	14·5	21	14	19·5
674	70			42	47	38·5	41·5

In order to determine the fraction of the methylene-blue adsorbed we made use of the following graphic method. The values of *b* were plotted as a function of the methylene-blue concentration for a definite wave-length, *e.g.*, $\lambda = 637\ \mu\mu$, and so also were the *ac* figures. From this graph (Fig. 2) the amount of adsorption for the various concentrations could be found.

The transmissive power, *b*, found for the methylene-blue (*e.g.*, for concentration 0·001%) has the same value as the calculated *ac* for the methylene-blue of concentration 0·00065%. This therefore indicates that 35% of the methylene-blue has been adsorbed by the yeast-phospho-protein particles and does not play any part in the light-absorption.

A source of error which must not be overlooked when working with methylene-blue in presence of products which have been isolated from living cells and tissues is the possible presence of fermentative substances capable of reducing the dye. In order to determine whether positive results (*i.e.*, disappearance of methylene-blue) were due to this cause we studied the change in the reduction of absorption with time.

The results showed (see Table II) that the change is not due to

TABLE II.

Influence of time on the adsorption.

Phospho-protein sol + Methylene-blue (0·0015%).

Time after mixing (hrs.).	0.		3.		4.		24.	
$\lambda(\mu\mu)$.	*ac.*	*b.*	*ac.*	*b.*	*ac.*	*b.*	*ac.*	*b.*
564	14·5	22·5	15·5	24	15·5	24·5	15·5	25
590	13·5	25	14·5	26	14·5	27	14·5	27
604	11	23·5	11·5	25	11·5	25·5	11·5	26
620	18·5	28	19·5	28·5	20	29·5	20	30

a fermentative reduction of methylene-blue, for the final values of the absorption are attained almost immediately after the solutions have been mixed. The subsequent change of absorption (*b*—*ac*), of the order of about 10% of the total absorption, is a phenomenon with which one has to reckon in all adsorption phenomena, and used to be described as static adsorption as contrasted with dynamic.

We have to thank Miss S. Rubinstein for help in the experimental part of the work.

THE HEBREW UNIVERSITY,
JERUSALEM.

[*Received, June 7th*, 1926.]

CCCV.—*A Critical Study of Ring Structure in the Sugar Group.*

By HARRY DUGALD KEITH DREW and WALTER NORMAN HAWORTH.

THE tendency of all aldoses to exist normally as amylene oxide forms has been shown to be a generalisation based on experimental results in the sugar group, and this generalisation has latterly been extended to the series of the ketoses (Charlton, Haworth, and Peat, this vol., p. 89; Haworth and Hirst, *ibid.*, p. 1858). To the unstable forms of sugars, the so-called γ-types, the butylene oxide structure has been allocated by one of us. It is of fundamental importance that these generalisations should be tested by adopting other methods of approach, and the object of the present communication is to show that if Hudson's "lactone rule" is extended to the sugars themselves, certain clearly-defined regularities occur supporting the generalisation as to the existence of the amylene oxide ring structure in the normal sugars. The results acquire an enhanced significance in view of the adverse

conclusions reached by Hudson in his most recent paper dealing with the ring system in glucose.

In the cases of twenty-four lactones derived from the sugar acids, Hudson (*J. Amer. Chem. Soc.*, 1910, **32**, 338) has shown decisively that ring formation occurs at the γ- (C^4) carbon atom, by observing the regularity, that, when the lactone is dextrorotatory, the hydroxyl group attached to the C^4 atom occurs on the right-hand side of the formula of the free acid (this formula being written with the carboxylic, or C^1, carbon atom at the top); while, when the lactone is lævorotatory, this hydroxyl group occurs on the left-hand side of the formula.

In these substances, it will be noticed, the C^1 carbon atom is symmetrical and has therefore no separate rotatory power, the dominating carbon atom, in this respect, apparently becoming the C^4 atom engaged in the ring closure.

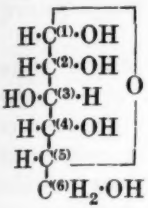
It appeared to us that, if the effect of the C^1 atom in the free sugars could similarly be eliminated, a comparison of the residual rotatory powers should throw new light on the types of ring structures obtaining in the sugars, the dominating carbon atom, in the rotatory sense, then becoming that which supplies from its hydroxyl group a hydrogen atom to the reducing group.

The C^1 atom in the free sugars, unlike that in the corresponding sugar acids and lactones, is asymmetric, its asymmetry giving rise to α- and β-forms of the sugars. If, however, the rotation of an equimolecular mixture of the α- and β-forms of a sugar can be observed or calculated, then, according to the principle of optical superposition, it may be considered that the effect of the C^1 atom has been eliminated, equal quantities of the α- and β-antipodal forms being present in a given weight of the sugar. The factor governing the sign of such a rotation will then, according to the foregoing considerations, be dominated substantially by the sign of the ring-forming carbon atom situated lower in the chain, and a comparison of the signs of the several carbon atoms in the chains of a series of sugars will enable the position of the ring-forming atom to be determined in individual cases.

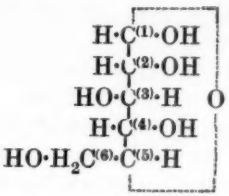
A preliminary examination of this hypothesis has been made in the present paper, and it may be said that the results indicate that valuable information can be obtained as to the types of ring structures present, at least in those hexoses in which the α- and β-forms are related in a normal manner.

In considering the formulation of sugar rings, it may be pointed out that the customary method of representation gives a picture which, in some respects, is a little misleading. Representing

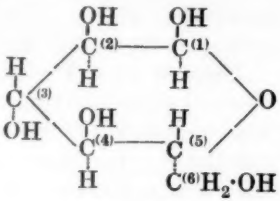
α-*d*-glucose, for example, as a 1 : 5 ring, formula (I) is conventional, the ring being said to be " on the right " of the formula.



(I.)



(II.)



(III.)

If, however, a model of such a structure be examined, it is found that with the usual stereochemical conventions (and assuming, in addition, that the links from oxygen are approximately tetrahedrally inclined), formula (II) affords a truer representation. In this formula, the laterally attached groups in the 1 : 5 chain may be considered to be in two parallel circles placed vertically in the paper, the 1 : 5 chain and the ring oxygen atom being in a third, and smaller, intermediate circle, which has C^3 as its nearest and O as its most remote point. A better arrangement is pictorially shown in (III), in which the formula has been placed on its side, so that the ring is now in the plane of the paper.

It will be noticed that, in the act of ring formation from the open-arc (aldehyde) formula, the C^5-hydroxyl group swings into the plane of the arc of the carbon chain, the C^5-hydrogen atom thus coming opposite the C^4-hydroxyl group, its place being filled by the C^6 atom and its addenda (formula II). A similar accommodating rotation or torsional movement occurs at the carbon atom carrying the ring-forming hydroxyl group whatever type of ring be produced, the hydrogen atom attached to this carbon atom always becoming transferred to the opposite side of the formula. Any carbon atoms of the chain not engaged in ring formation must be considered to lie in a further arc, inclined to the plane of the ring, and to be possessed of possible free rotation.

It will be clear that, when the ring-forming carbon atom is not asymmetric (as, for example, in the case in which an aldopentose is considered to form a 1 : 5 ring), the ring-forming carbon atom can no longer dominate the rotatory power of the equimolecular mixture of the α- and β-forms of the sugar. For the present, therefore, only those cases in which this atom is presumed to be asymmetric will be considered. It may be remarked, however, that if a regularity be discovered in the latter cases, the absence of such a regularity in the former series affords an indication that a symmetrical

carbon atom has become engaged in the ring formation. In the cases of the aldopentoses and ketohexoses, for example, such evidence would be decisive, there being only one such hydroxyl-bearing carbon atom within the molecule.

There is no difficulty in calculating the specific rotation of an equimolecular mixture of the α- and β-forms of a given sugar where rotations of these forms have been separately observed or calculated. In other cases, in which the equilibrium rotation of the sugar is known and the rotation of one of the forms has also been observed, it has been assumed that the equilibrium mixture consists of the α- and β-forms in the approximate ratio of 2 : 3 (Hudson, *J. Amer. Chem. Soc.*, 1909, **31**, 71). Although this ratio is subject to some variation, it is considered sufficiently exact to lead to results indicating the correct sign of rotation in all but exceptional cases.

If, as has been suggested (Charlton, Haworth, and Peat, *loc. cit.*), glucose, galactose, and mannose exist normally as 1 : 5 ring forms (amylene oxides), then, assuming the truth of the foregoing hypothesis, the sign of the specific rotation of an equimolecular mixture of the α- and β-forms of any one of them should be the same as that of the C^5 carbon atom. The configurations in the sugar series and in the corresponding lactones happen so to have been chosen that the sign of the C^5 atom is found to be positive when the attached hydroxyl group is on the right of the formula written as the open-chain form (aldehyde form), or when the attached hydrogen atom is on the right of the formula written as the ring form as in (II).

It will also be clear that if a 1 : 5 ring is persistently formed in ascending to the higher series from a given sugar, the successive signs of rotation of the equimolecular mixtures of α- and β-forms of the ascending series of that sugar will be the same as the successive signs of the C^4, C^3, C^2 carbon atoms in the parent sugar. Thus, the sign in the case of glucose should be positive; in glucoheptose, positive; in gluco-octose, negative; and in gluconononose, again positive. In other words, the alternation of sign in such an ascending series will reflect the alternation in configuration of the successive carbon atoms in the parent sugar.

The same considerations will apply if the rings be considered as 1 : 4, 1 : 3, or 1 : 2 rings, the alternation then occurring from the C^4, C^3, or C^2 atoms towards C^1.

If then the successive signs for the actual rotations, found or calculated, do not agree with those deduced on the assumption of the presence of a particular type of ring, its presence may be regarded as improbable. It is shown in Table I that the only type

of ring which gives results in accord with this deduction is, in the case of glucose, galactose and mannose, the 1 : 5 ring (amylene or δ-oxide ring); and that the assumption of the presence of this ring enables the correct sign of rotation to be deduced in every case in which sufficient data are available for the test.

TABLE I.

	Specific rotation.				Sign deduced on the assumption of			
Sugar.	α-Form.	β-Form.	Equimol. mixture.	Sign found.	1 : 5 ring.	1 : 4 ring.	1 : 3 ring.	1 : 2 ring.
d-Glucose.	+113°	+19°	+66°	+	+	+	−	+
d-α-Glucoheptose.	+ 45	−28	+ 8·5	+	+	−	+	
d-α-Gluco-octose.	+ 4(c)	−86	−41	−	−	+		
d Glucononose.	(Sp. rot. of sugar +13°.)			?	+			
d-Galactose.	+144	+52	+98	+	+	−	−	+
d-β-Galaheptose.	− 22	−75 (c)	−48·5	−	−	−	+	
d-Galaoctose.	(Sp. rot. of sugar above −40°.)			?	−	+		
d-Mannose.	+ 30	−17	+ 6·5	+	+	+	−	−
d-Mannoheptose.	+ 85	+58 (c)	+71·5	+	+	−	−	
d-Manno-octose.	(Sp. rot. of sugar − 3°.)			?	−	−		
d-Mannononose.	(Sp. rot. of sugar +50°.)			?	−			

(c) Indicates a calculated figure.

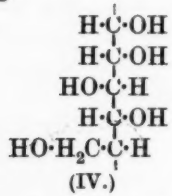
It will be observed, on scrutiny of Table I, that, of seven cases in which the data are available, all are in agreement with that of a 1 : 5 ring while only three are in agreement with that of a 1 : 4 ring. In addition, in the case of each of the three sugars, the correct alternation of sign is found for the ascending series only on the assumption of the 1 : 5 ring. Of the four cases in which the data are insufficient, three appear to be in favour of the 1 : 5 ring—so far as can be judged from the signs of the rotation of the sugars themselves (equilibrium mixtures); the sole exception, *d*-mannononose, is a substance of which the nature is considered to be in doubt (Fischer, " Untersuchungen über Kohlenhydrate und Fermente," p. 582).

In the case of mannose, however, we had concluded, from other considerations, that the relationship between the α- and β-forms was not a normal one, and this conclusion has recently been expressed in definite terms by Hudson (*J. Amer. Chem. Soc.*, 1926, **48**, 1427). The figures quoted for *d*-mannose and *d*-mannoheptose must therefore be regarded with caution, although it is not considered probable that revision will alter the signs given for the rotations of the equimolecular mixtures of the α- and β-forms.

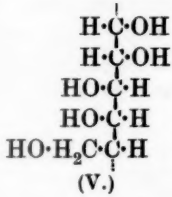
The case of *l*-rhamnose is similarly doubtful (Hudson, *loc. cit.*), and therefore need not be considered at present.

Formulæ (IV), (V) and (VI), in which the α-forms of *d*-glucose, *d*-galactose and *d*-mannose are represented, respectively, as 1 : 5 rings in accordance with the method already indicated (compare formula II), will serve to make clear the deductions contained in Table I.

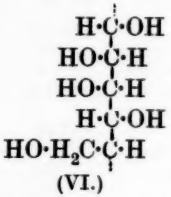
In the succeeding formulæ, the part of the ring corresponding with that shown dotted in formula (II) will be omitted, the oxygen atom being supposed always to lie below the plane of the paper, and only those carbon atoms in the central chain being within the ring.



(IV.)



(V.)



(VI.)

In Table II are shown values for six derivatives of *d*-glucose and *d*-galactose, the assumption of a 1 : 5 ring in each case agreeing with the sign of rotation found.

TABLE II.

Sugar.	Specific rotation. α-Form.	Specific rotation. β-Form.	Equimol. mixture.	Sign found.	Sign deduced for 1 : 5 ring.	1 : 4 ring.	1 : 3 ring.	1 : 2 ring.
d-Methylglucoside.	+159°	−34°	+62·5°	+	+	+	−	+
d-Ethylglucoside.	+150	−33	+58·5	+	+	+	−	+
d-Glucose penta-acetate.	+102	+ 4	+53 (in $CHCl_3$)	+	+	+	−	+
d-Methylglucoside tetra-acetate.	+136	−22	+57 (in MeOH)	+	+	+	−	+
d-Methylgal-actoside.	+179	(very small)	+89·5	+	+	−	−	+
d-Ethylgal-actoside.	+186	− 4	+91	+	+	−	−	+

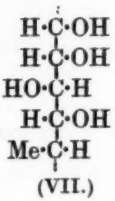
Finally, the cases of *d-iso*rhamnose (VII), fucose (VIII), and *l*-α-rhamnohexose (IX) are shown in Table III. (The formulæ show α-forms.)

TABLE III.

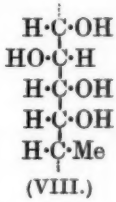
Sugar.	Specific rotation. α-Form.	Specific rotation. β-Form.	Equimol. mixture.	Sign found.	Sign deduced for 1 : 5 ring.	1 : 4 ring.	1 : 3 ring.	1 : 2 ring.
*d-iso*Rhamnose.	+ 73°	+ 1·3° (c)	+37°	+	+	+	−	+
Fucose.	−124	−42 (c)	−83	−	−	+	+	−
l-α-Rhamno-hexose.	− 83	−47(c)	−65	−	−	+	+	−

(c) Indicates a calculated figure.

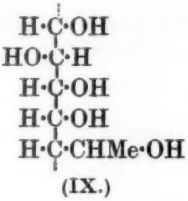
Here, again, the 1 : 5 ring is the only type which affords agreement between the actual and deduced signs of rotation in all three cases.



(VII.)



(VIII.)



(IX.)

The agreement in the examples given can scarcely be due to coincidence alone, and it is therefore concluded that a strong preliminary case has been made out in favour of the view that amylene or δ-oxidic rings are present normally in the cases of the sugars mentioned, their higher analogues, and probably also in the cases of the remaining aldohexoses. If this be the case, then it follows also that the carbon atoms dominating the rotatory power of a sugar are those on either side of the ring oxygen atom, and that attention should be focussed principally on these in making deductions from the rotatory power as to the structure of the polysaccharides. When one of this pair of carbon atoms is symmetrical, it may follow that the remaining asymmetric carbon atom has a principal effect.

In a recent paper (*loc. cit.*, p. 1434), Hudson has criticised the conclusion of Charlton, Haworth, and Peat (*loc. cit.*) that glucose and the methylglucosides possess 1 : 5 rings. From a comparison of the rotatory powers of certain related sugars, Hudson concludes that the α- and β-methylglucosides and β-methyl*iso*rhamnoside contain 1 : 4 rings. His proof in the case of α-methyl-*d*-glucoside is based on a comparison between α-methyl-*d*-galactoside and β-methyl-*l*-arabinoside on the one hand, and α-methyl-*d*-glucoside and α-methyl-*d*-xyloside on the other, when these substances are written as 1 : 5 rings. Since, on chemical grounds, it is considered that methyl-xyloside, -arabinoside and -galactoside have 1 : 5 rings, and since α-methylglucoside has a rotation not in accordance with that calculated if glucose be placed in this ring series, Hudson concludes that the glucosides possess 1 : 4 rings. Exception may well be taken, however, to a method which assumes that the C^4 atom has the same rotational value in the pentoside and hexoside structures considered as 1 : 5 rings; because, in the former this C^4 atom is joined to one symmetrical and one asymmetric carbon atom, whilst in the latter it is joined to two asymmetric carbon atoms. If the hypothesis considered in the present paper contains a

measure of truth, the probability follows that in the above two series the C^4 carbon atom has a widely different rotational significance.

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CCCVI.—*An X-Ray Study of Some Structural Modifications of Long-chain Compounds.*

By STEPHEN HARVEY PIPER, THOMAS MALKIN, and HAROLD E. AUSTIN.

THERE is now considerable evidence showing that in several homologous series of long-chain compounds a linear relation exists between the length of the chain of carbon atoms and an important crystal-spacing which is comparable with the length of the molecule. It is tempting to employ measurements of these long spacings as a means of identification of such compounds: in fact, several successful analyses have been made (Robinson, *Nature*, 1925, **116**, 45; Trillat, *Compt. rend.*, 1925, **180**, 1330; Piper, Brown, and Dyment, J., 1925, **127**, 2194). We have found, however, that there are modifications and distortions in many substances which may cause the *X*-ray measurements to be very misleading, and a systematic study is now described of the following three effects:

(1) Alternative forms of the same substance.

(2) Distortions caused by mounting the specimen for *X*-ray examination.

(3) The influence of impurities on crystal-spacing.

(1) *Alternative Forms of Fatty Acids.*

With one exception all the fatty acids we have examined give *X*-ray photographs which show that they can exist in at least two forms, each having its own long spacing. It has already been found by Müller (J., 1925, **127**, 602) that the normal paraffin hydrocarbons, when kept at suitable temperatures, show two alternative long spacings. The spacings we have found for the fatty acids, however, are independent of the temperature, the value obtained depending only on the treatment followed in mounting the specimen, and on the manner of preparation of the acid.

It is not easy to obtain large single crystals of these acids for study by the usual methods, but, as Müller has shown (J., 1923, **123**, 2043), if a thin layer of the substance is melted on a glass strip, the planes it is wished to measure lie parallel to the surface of the glass. This author finds that the same effect is obtained by pressing

TABLE I.

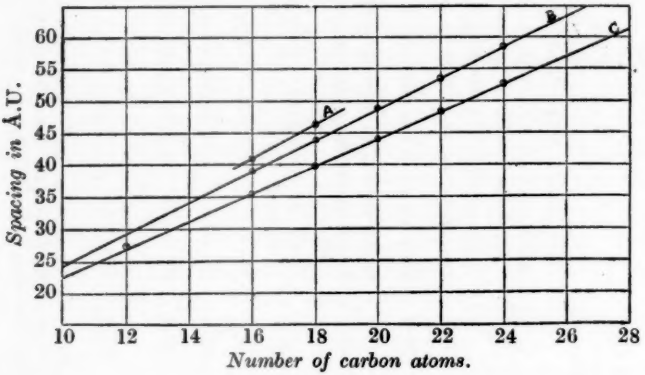
Acid.	Formula.	M. p.	Spacings (Å.U.). Pressed.	Spacings (Å.U.). Melted.	Method of preparation.
Lauric.	$C_{12}H_{24}O_2$	44·5°	27·4	—	Kahlbaum's (*K*) purified by crystallisation from dilute ethyl alcohol.
Palmitic (*K*).	$C_{16}H_{32}O_2$	64	41·0 *w* 35·6 *s*	35·65	Kahlbaum's (*K*). Ethyl ester fractionated and hydrolysed; acid finally crystallised from acetone and from benzene.
Palmitic (*K*).			39·08		Single crystal of preceding specimen.
Palmitic (*O*).		63·5	35·7	35·7	Potash fusion of potassium oleate.
Stearic (*K*).	$C_{18}H_{36}O_2$	71	46·6 *s* 39·9 *w*	39·9	Purified as in the case of palmitic acid (*K*).
Stearic (*K*).			43·98		Single crystal of preceding specimen.
Stearic (*O*).		71	44·0	40	Ethyl oleate fractionated, and reduced with H_2 in presence of colloidal Pd.
Eicosanic.	$C_{20}H_{40}O_2$	75	49·0 *s* 44·3 *w*	44·2	From Dr. Steuwer. Potash fusion of erucic acid (Ehrenstein and Steuwer, *J. pr. Chem.*, 1922—23, **105**, 199).
Eicosanic.		75	44·1	44·1	From Prof. Morgan. Same method as above (*J.S.C.I.*, 1924, **43**, 347T).
Behenic.	$C_{22}H_{44}O_2$	81	53·7 *s* 48·5 *s*	48·6	By reduction of erucic acid.
Tetracosanic.	$C_{24}H_{48}O_2$	83·5	58·5	52·8	From Dr. Brigl. Synthesised from behenic acid (*Z. physiol. Chem.*, 1922, **119**, 280).
Lignoceric.	$C_{24}H_{48}O_2$	83·4	58·4 *s* 52·9 *w*	52·7	From Dr. Brigl (*loc. cit.*). From beechwood tar.

The apparatus used for the fractionation of the above esters is described by Armstrong, Allan, and Moore (*J.S.C.I.*, 1925, **44**, 65T), and consists of a distillation flask provided with a two-bulbed neck packed with glass beads. The following data were obtained: Ethyl palmitate, b. p. 157°/2 mm., 154°/1·5 mm.; ethyl stearate, b. p. 182°/2 mm.; ethyl oleate, b. p. 172°/2 mm., $n^{15°}$ 1·4536; ethyl erucate, b. p. 218°/3 mm., 247°/12·5 mm.

flakes of compounds that crystallise in plates on the glass strip, and Trillat (*loc. cit.*) has obtained brilliant photographs from films formed by evaporating a few drops of an alcoholic solution on a plate. We have used all three types of layer.

Generally speaking, a pure crystalline acid, when pressed on a plate with only sufficient force to cause the flakes to adhere with the minimum breakage, gives a photograph showing two sets of lines (Plate I). One set is due to the spacing discovered by Müller (*loc. cit.*, 1923), and we have called this the " C " spacing. The other lines, " B," arise from more widely separated planes. When the acid is *melted* on the mount the " C " lines alone appear, and in some cases the pressed flakes have given only " C " or only " B "

FIG. 1.



lines. In Table I, spacings that are bracketed have been photographed simultaneously, and the relative strengths of the lines given by each are indicated by the letters *w*, weak, or *s*, strong. We have obtained specimens from the greatest possible variety of sources, used as many methods of preparation as possible, and sought a very high degree of purity. Our grateful thanks are due to the various donors of material whose names appear in col. 6 of Table I. The m. p.'s were obtained with a standard Anschütz thermometer.

In Fig. 1, the spacings from Table I are plotted against the number of carbon atoms in the molecule, and it will be seen that, with two exceptions, they lie on the two non-parallel straight lines B and C. Of these lines, C is that given by Müller, who showed that it could be accounted for by assuming that the spacings were due to planes separated by the lengths of two molecules placed end to end, and that the carbon atoms occupied a mean length of 1 Å.U. in the chain. On the same grounds, the type of chain that will give a " B " spacing requires an effective chain length of 1·21 Å.U. per carbon atom,

PLATE I.

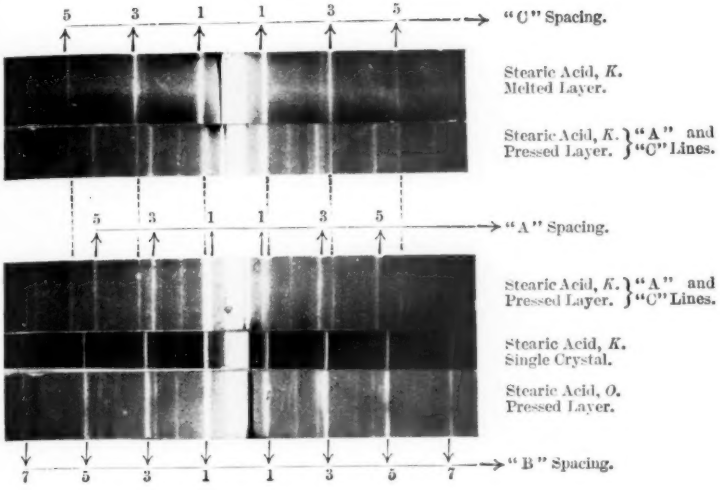
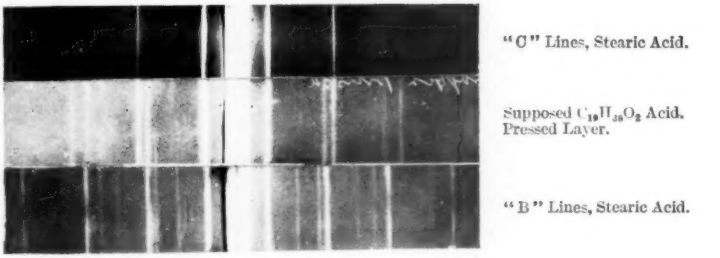

5 3 1 1 3 5
"C" Spacing.
Stearic Acid, K. Melted Layer.
Stearic Acid, K. Pressed Layer.
"A" and "C" Lines.
5 3 1 1 3 5
"A" Spacing.
Stearic Acid, K. Pressed Layer.
"A" and "C" Lines.
Stearic Acid, K. Single Crystal.
Stearic Acid, O. Pressed Layer.
7 5 3 1 1 3 5 7
"B" Spacing.

PLATE II.



[*To face page* 2312.]

and is probably a co-planar zig-zag of atoms with the lines joining successive centres inclined at an angle of 109° 28′ (Müller and Shearer, J., 1923, **123**, 3159).

The " B " spacing is the true (single) crystal-spacing; it appears to be due to the type of chain assumed by the molecule when the pure acid crystallises slowly. The " C " spacing is always found when the crystallisation has taken place rapidly or under constraint, as in the case of acids melted on glass or of the rapidly-evaporated films studied by Trillat. We find also that the presence of an impurity causes the acid to assume the " C " form (see section 3). The difference between the two forms does not appear to be inherent in the molecule, but is rather due to external causes that have affected the crystallisation.

In addition to these " B " and " C " spacings, both stearic and palmitic acids obtained from purified Kahlbaum acids and carefully pressed on a glass plate have given lines due to a still larger " A " spacing. The lines are most marked in the case of stearic acid, and are shown in Plate I in company with the fainter " C " lines that were photographed simultaneously. Below this photograph are shown the lines due to the " B " spacing obtained from a large single crystal of the same specimen of acid, and from another specimen that was prepared from oleic acid. The last two show only the " B " lines, although the acids have identical m. p.'s. We at first attributed the " A " spacing to the single crystal, and thought that perhaps the " B " spacing occurred when the acid had been prepared from a substance containing doubly-linked carbon atoms, but we eventually obtained large single crystals from both the Kahlbaum stearic and palmitic acids and found that they had the " B " spacing. The " A " lines on the stearic acid photograph (Plate I) cannot well be attributed to impurity—they are too strong and too permanent. To test the permanence of this form the acids were again esterified, and the esters redistilled and reconverted to the acids. There was no change in the m. p.'s, and when the flakes were pressed on glass the photograph again showed the " A " lines in company with the " C," but, if anything, more strongly. When the acids were melted on the mount, the " C " lines only appeared as before. In the case of palmitic acid the " A " lines are weak, but very persistent. The difference between the " A " spacings for palmitic and stearic acids is 5·6 Å.U., which means that, if this is a third type of chain, each carbon atom in it occupies an effective length of 1·4 Å.U. This is approximately the size of a carbon atom in the chain typical of a normal hydrocarbon, *i.e.*, 1·3 Å.U. It is noticeable that, though both " A " and " C " or " B " and " C " spacings occur simultaneously, we have not obtained " A " and " B " on the same plate.

It seems therefore that the chains giving rise to the " A " and " B " spacings are different in the molecule itself, and are not due to conditions affecting the crystallisation. It will also be noticed that the spacing 46·5 Å.U. falls on the B graph at 19 carbon atoms, and on the C line at 21 carbon atoms. This is fortuitous; it does not indicate the presence of either a $C_{19}H_{38}O_2$ or a $C_{21}H_{42}O_2$ acid, since the spacings of odd- and even-numbered acids do not correspond.

Two specimens of stearic acid (*O*, Table I) were prepared by the reduction of ethyl oleate. In one case the ester was fractionated and in the other the acid was purified by crystallisation alone, but in both cases the photographs showed only " B " lines for crystal flakes and only " C " lines when the acid was melted.

Stearic acid has the same m. p. in the three forms that give rise to the " A," " B," and " C " spacings, and in each form the crystalline planes are separated by the length of two molecules. It is probable, therefore, that the linkages of the carboxyl groups are very similar in the three forms. The linear relation between the " B " spacings and the number of carbon atoms probably breaks down sooner than that between " C " spacings and the carbon content, since the slope of the graph is such as to give a negative intercept on the axis of spacings. The evidence definitely suggests that the higher members of the fatty-acid series exist in two forms, " B " and " C," each having its characteristic chain, and that palmitic and stearic acids have yet a third form. It is hoped to obtain more information on the " A " spacings from a series of acids synthesised from the Kahlbaum (*K*) stearic acid.

(2) *Distortions due to Mounting.*

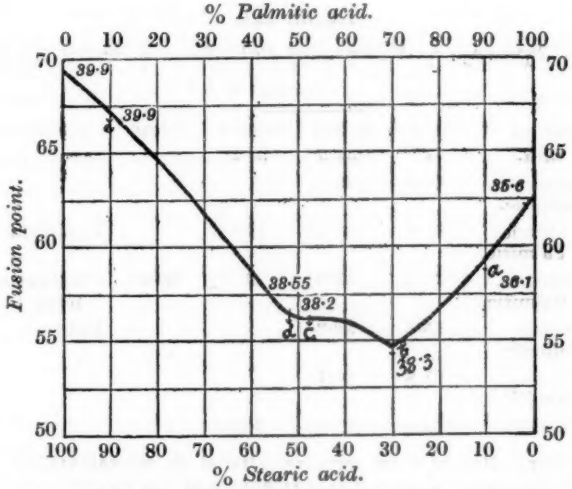
Data published by different observers for spacings of the same substance appear to differ by amounts greater than the probable experimental error. In Table II are a number of measurements of the spacings of five pure long chain compounds mounted in the three ways mentioned in section (1), and it will be seen that some of the differences mentioned may be due to varying technique. The spacings are in most cases calculated from five measured orders, and the different orders on the same plate agree to about 0·2%. Pressed crystals, which give more orders and denser lines, usually show the best agreement.

Pressed and melted hydrocarbons show the greatest variation with treatment. It is possible that the different spacings are due to modifications comparable with the " A," " B," and " C " type of the fatty acids, but on the whole the evidence indicates a distortion of the lattice increasing in amount with the degree of intimacy of contact with the mounting, since the spacings of the melted form

TABLE II.

Substance.	M. p.	Solvent.	Spacings in Å.U. Melted.	Pressed.	Evap.
Triacontane.	66°	Benzene.	40·7	40·3	—
		Ether.	40·8	40·4	—
Tetracosane (from paraffin wax).	51·9	Benzene.	33·4	32·7	33·15
		Ether.	33·4	32·86	—
		Acetone.	33·45	32·86	—
Ethyl palmitate.	25	Petrol. Ether.	23·2	22·95	23·2
Palmitic acid.	64	Acetone.	35·6	35·65	—
		Ether.	35·54	35·7	—
Thallium palmitate.	115	Alcohol.	38·8	38·7	—

FIG. 2.



Mixed melting points; palmitic–stearic acids (de Visser).

(The figures on the curve are the "C" spacings in Å.U. *shown in Table III.)*

differ more from those of the pressed than from those of the evaporated forms. All the first three substances have one molecule between the planes; the acid and the soap have two, and it appears that the former class is the more easily distorted. As would be expected the solvent has no influence on the crystal spacing, and the nature of the mount, so far as we have examined it, has no important influence on the amount of distortion.

These variations must be not confused with the alternative spacings described by Müller for the normal hydrocarbons.

We are indebted to Mr. Dennis Brown for taking several of the photographs involved in Table II.

(3) *The Influence of Impurities.*

The system studied is a mixture of the carefully purified palmitic and stearic acids (Table I). De Visser has made a study of the mixed m. p.'s of these acids (*Rec. trav. chim.*, 1898, **17**, 182); they were therefore selected in preference to more widely-separated acids; a few mixtures of such acids have also been photographed.

Fig. 2 is a reproduction of de Visser's fusion-point curve, and on it are marked the mixtures, *a*, *b*, *c*, *d*, and *e*, that were photographed. A melted layer was used in each case, and mixture *c*, which de Visser states to be a constant-crystallising mixture, was also examined in the form of crystal flakes and when evaporated. The results are shown in Table III.

TABLE III.

"C" Spacings of Mixtures of Palmitic and Stearic Acids.

	Composition.	M. p.	Spacings in Å.U. Melted.	Pressed.	Evap.	Notes.
	Stearic acid.	71°	39·9	39·9		
e.	90% Stearic. 10% Palmitic.	68·8	39·9			
d.	52·6% Stearic. 47·4% Palmitic.	57·6	38·55	39·6*		Equimolar.
c.	47·5% Stearic. 52·5% Palmitic.	57·3	38·2	39·6*	39·6	Constant-crystallising (?).
b.	30% Stearic 70% Palmitic.	55·4	38·3			Eutectic.
a.	10% Stearic. 90% Palmitic.	61·8	36·1			
	Palmitic acid.	64	35·65	35·6		

* The composition of these mixtures altered on crystallisation; the proportion of stearic acid increased in *d* to 65% and in *c* to 55%.

Morgan and Bowen (*J. Soc. Chem. Ind.*, 1924, **43**, 348 T) state that certain binary higher saturated fatty-acid mixtures show evidence of the formation of compounds of one molecule of each acid. It was of interest, therefore, to examine such an equimolecular mixture, since if the double molecule consists of one stearic and one palmitic chain with the carboxyl groups in contact, the *X*-ray spacing should be the mean of the spacings of the two pure acids. The value obtained is too high for this interpretation.

In the case of the *c* mixture the spacings obtained from the three different types of mounting varied so considerably that we were led to examine it more closely. We are convinced that this is not a constant-crystallising mixture, and that such a mixture does not exist, since when alcohol, benzene, or acetone is used as a solvent,

the mixture in each case becomes richer in stearic acid on crystallisation.

Whilst the spacing obtained from any given melted mixture appears to depend slightly on the conditions under which the layer is formed (rate of cooling, etc.), it may be stated that the photograph, will, as a rule, show a distorted spacing of the longer chain, except for high proportions of the lower acid when it approaches the shorter chain. We have not obtained any plates showing the lines of both stearic and palmitic acids, but with more widely separated acids, such as lauric and behenic or lauric and palmitic acids, a photograph from a melted layer shows the spacings due to the chains of each acid with apparently very little distortion. The plates are usually faint and show only first- and third-order lines.

When either *c* or *d* mixture was crystallised from alcohol by complete evaporation of the solvent, the crystals obtained were small but looked satisfactory. The m. p.'s were 58·5° and 61·5° respectively. If these crystals were pressed on a glass plate the photograph still showed only one set of lines, the " C " lines of stearic acid almost undistorted. It is very remarkable that such impure mixtures should give a photograph indistinguishable from that of a pure acid except for the small number of orders. It is easier to explain the distorted spacing of the melted-mixture plates, where the particular acid in excess of the eutectic proportion will separate first as the mixture cools, and cannot be expected to crystallise normally in the presence of a quantity of impure molten acid. The 90% palmitic acid mixture differs more from pure palmitic acid than does the 90% stearic acid from pure stearic acid, as would be expected, since the former is much closer to the eutectic proportions.

The difficulty of interpreting an *X*-ray photograph is well illustrated by the following example. The acid in question was obtained from the oxidation products of paraffin wax *; it had m. p. 58° and an acid value corresponding to $C_{19}H_{38}O_2$, and it crystallised in beautiful flakes. The *X*-ray photograph obtained from a layer of these flakes pressed on a glass plate is reproduced in Plate II, together with a plate of the " C " stearic acid lines above, and the " B " stearic lines below. The spacings calculated are 43·8 and 39·9 Å.U., practically the " B " and " C " spacings of stearic acid. When the acid was melted, only the spacing of 39·9 appeared. Except for the fact that the value of 43·8 differs rather more from the " B " spacing of stearic acid than we should expect, this is what a pure specimen of stearic acid may give. The m. p. and the acid value make it obvious

* A complete account of other acids from the same source will be communicated later.

that this cannot be the correct explanation. It is, however, possible that the value of 43·8 is a distorted version of the "C" spacing of eicosanic acid, and the presence of this acid as an impurity would explain both the acid value and the m. p. This is very likely the correct explanation, although it is difficult to reconcile it with the results obtained from mixed stearic and palmitic acids, in which both crystalline and melted mixtures showed only the longer chain, but here we have the case of both spacings for the mixed crystals and the *shorter* chain for the melted layer. The data published for the odd-numbered acids are not very satisfactory, and it is possible that more detailed information from pure synthetic odd-numbered acids will throw some light on this anomalous behaviour. It is also possible that the behaviour of mixed stearic and palmitic acids is not typical. It is, however, clear that the evidence from *X*-ray photographs must be used with great caution; it is, for example, easy to confuse the "C" spacing of eicosanic acid with the "B" spacing of stearic acid, unless the conditions of the experiment are studied.

Summary.

X-ray measurements show that the higher fatty acids have at least two forms of chain, of which the longer is that appearing in the true single crystal. The longer chain is always converted to the shorter when the acid is fused, but there is no difference in the m. p.'s of the two forms. Stearic and palmitic acids appear to have three possible chains.

Measurements of the long crystal spacings must be employed as a means of identification with great care, since not only may the crystals exist in two or more forms, but in many cases they are easily distorted by treatment in mounting and by the presence of impurity, especially if the impurity is similar in nature and has nearly the same number of carbon atoms in the molecule.

These experiments were carried out with the aid of a grant from the University of Bristol Colston Research Society.

THE UNIVERSITY, BRISTOL. [*Received, June 12th,* 1926.]

CCCVII.—*The Electrolytic Synthesis of Tetramethyladipic Acids.*

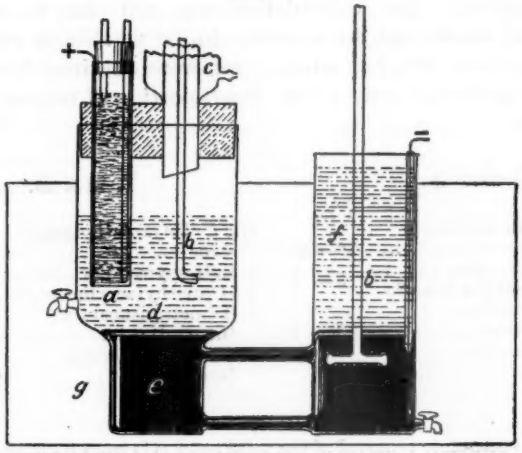
By ERNEST HAROLD FARMER and JACOB KRACOVSKI.

THE preparation of ββ′β′-tetramethyladipic acid by ordinary synthetic methods has been the subject of prolonged experiment. There are no naturally occurring substances from which this acid

may be derived and all attempts to synthesise it from substances such as *s*-tetramethylethylenedibromide, β-iodo*iso*valeric acid and ββ-dimethyl-lævulic acid have failed. No adipic acid containing two *gem*-dialkyl groups has hitherto been obtained, yet the interest attaching to these and other polyalkyladipic acids in connexion with the strain theory is such that experiment has been continued in the direction of synthesis by electrolysis.

The ease with which adipic ester may be obtained electrolytically from ethyl sodium succinate rendered it probable that reasonable yields of the αα′α′-tetramethyladipic acid would be obtainable by

FIG. 1.



(a) *Platinum anode sealed into glass tube provided with inflow and outflow tubes;* (bb) *stirrers;* (c) *water condenser provided above with mercury seal and side-arm for use when collecting more volatile products;* (d) *electrolyte;* (e) *mercury cathode;* (f) *alcohol;* (g) *water-bath.*

employing the sodium salt, $CO_2Et{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2Na$ (I); consideration of the isomeric compound $CO_2Et{\cdot}CH_2{\cdot}CMe_2{\cdot}CO_2Na$ (II), would suggest, however, the great probability of degradation to β-methyl*iso*crotonic ester (III), or the isomeric ββ-dimethylacrylic ester, rather than to a coupling of the residues to yield (IV):

$$2CO_2Et{\cdot}CH_2{\cdot}CMe_2{\cdot}CO{\cdot}O\cdots \begin{cases} \nearrow 2CO_2Et{\cdot}CH_2{\cdot}CMe{:}CH_2 \text{ (III.)} \\ \searrow CO_2Et{\cdot}CH_2{\cdot}CMe_2{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2Et \text{ (IV.)} \end{cases}$$

Nevertheless, the electrolysis of the sodium salts of both ethyl hydrogen *as*-dimethylsuccinates has been effected, and in each case the appropriate tetramethyladipic acid has been obtained. The yields, however, were very different in the two cases.

In selecting an apparatus suitable for the continuous electrolysis

of large quantities of material, that of Bouveault (*Bull. Soc. chim.*, 1903, [3], **29**, 1042) was taken as a pattern in designing the less expensive and more convenient form shown in the diagram. The requisite low temperature and high current density (50—100 amps./dcm.^{2}) at the anode were readily obtained, and owing to the nature of the cathode and circulatory system (securing a continuously changing mercury surface), the anions were so efficiently removed that little hydrolysis occurred in the alcoholic electrolyte.

The products obtained from esters (I) and (II) are shown in Tables A and B respectively. A large proportion of the material suffered severe degradation leading to volatile products which were not investigated. This degradation was not due to unsuitable experimental conditions, since under similar conditions consistently good yields (over 70%) of adipic ester were obtained from methyl sodium succinate and only a very small portion of material suffered degradation.

TABLE A.

	%
aaa'a'-Tetramethyladipic ester	32—35
Methoxypivalic ester (?) / *ββ*-Dimethylacrylic ester*	3— 5
as-Dimethylsuccinic (neutral) ester	5— 7
as-Dimethylsuccinic (acid) ester	17
	62

TABLE B.

	%
βββ'β'-Tetramethyladipic ester	5— 8
β-Methoxy*iso*valeric ester	8—10
ββ-Dimethylacrylic ester	30—35
as-Dimethylsuccinic (neutral) ester	Trace.
as-Dimethylsuccinic (acid) ester	11
	61

* Since the complete removal of the solid ester (II) from its liquid isomeride (I) could not be attained with certainty, the appearance of this substance is probably to be attributed to this cause.

The appearance of ethyl ββ-dimethylacrylate rather than of ethyl β-methyl*iso*crotonate among the products from (II) affords another instance of the apparent inability of the latter to exist in a free state.

EXPERIMENTAL.

as-*Dimethylsuccinic Anhydride.*—Large quantities of dimethylsuccinic acid were obtained by the method of Thorpe and Higson (J., 1906, **89**, 1463), the yield of pure acid being 40—45%. Heating for 3 hours with acetyl chloride (three times theory) and subsequent distillation yielded the anhydride (b. p. 111°/16 mm.) in crystalline form.

Ethyl Hydrogen as-*Dimethylsuccinate.*—The anhydride was refluxed for 4 hours with twice the theoretical amount of alcohol. After removal of excess of alcohol the ester (II), m. p. 68°, crystal-

lised out and was removed by filtration and recrystallised from petroleum; the residual oil which yielded further small crops of crystals on dilution and strong cooling was freed from traces of neutral ester and distilled. It was obtained as a colourless oil, b. p. 147°/15 mm., which on long standing deposited a further small quantity of the crystalline isomeride. This substance was no doubt identical with de Rosanbo's acidic ester (*Ann. Chim.*, 1923, [ix], **19**, 335) [Found: C, 54·6; H, 7·6; *M* (monobasic), 174. Calc. for $C_8H_{14}O_4$: C, 55·1; H, 8·0%; *M*, 174].

Electrolysis of Ester (II).—The ester (174 g.), dissolved in a small amount of methyl alcohol, was gradually added to a cold alcoholic solution of sodium hydroxide obtained by dissolution of sodium (23 g.) in methyl alcohol (230 g.) and addition of water (18 g.). The resulting fine suspension of sodium salt was electrolysed in two portions (*C.D.* about 70 amps./dcm.^{2}). The temperature of the liquid rose appreciably but in the immediate neighbourhood of the anode it remained at 18°. After about 20 hours, the current fell to zero and the clear solution was removed. The methyl alcohol was distilled off and the residue poured into water. The precipitated oil was extracted with ether and the ethereal solution shaken with dilute alkali. The alkaline extract yielded the original acidic ester (15 g.); the ethereal solution contained a mixture of neutral oils which was carefully fractionated, the lower-boiling fractions being redistilled at atmospheric pressure. Ultimately three main fractions were obtained of b. p. 145—148° and 172—174° at atmospheric pressure, and 145—150°/16 mm., respectively. The products of the various electrolyses showed slight variations in the relative proportions of the different fractions, but the total yield did not vary appreciably.

ββ-*Dimethylacrylic Acid*.—The ester fraction, b. p. 145—148°, which possessed the characteristic odour of dimethylacrylic ester, was hydrolysed by boiling for 1½ hours with the calculated amount of 50% aqueous potash to which sufficient alcohol had been added to bring the oil into solution. After removal of alcohol and traces of unchanged ester by ethereal extraction of the diluted alkaline product, the acid was obtained in almost pure condition on acidification and re-extraction. It was crystallised from water as long needles, m. p. 69°, and was in all respects similar to authentic ββ-dimethylacrylic acid.

β-*Methoxyisovaleric Acid*.—Hydrolysis of the ester fraction, b. p. 172—174°, under similar conditions yielded a syrupy acid, b. p. 118°/14 mm., which was readily soluble in water [Found: C, 55·1; H, 8·8; *M* (monobasic), 130. $C_6H_{12}O_3$ requires C, 54·5; H, 9·1%; *M*, 132]. The ester of this acid was not directly con-

vertible into ββ-dimethylacrylic acid by treatment with phosphorus trichloride, followed by hydrolysis. Estimation of the methoxyl group in the acid (Zeisel method) indicated the constitution assigned.

ββββ′β′-Tetramethyladipic Acid.—The ester fraction, b. p. 145—150°/16 mm., was boiled with 6 times its volume of concentrated hydrochloric acid until hydrolysis, which was effected slowly and with some charring, was complete. On cooling, the solution deposited crystals of a saturated acid, m. p. 207—208°. This substance was moderately soluble in benzene, ether and hot water, crystallising from the last in long prisms [Found : C, 59·3; H, 9·0; *M* (dibasic), 204. $C_{10}H_{18}O_4$ requires C, 59·4; H, 8·9%; *M*, 202]. This acid, unlike the αα′α′-acid, could readily be brominated by successive treatment with phosphorus pentachloride and bromine. The hydrolysis liquor on further evaporation yielded a small quantity of tetramethyladipic acid and some *as*-dimethylsuccinic acid.

Electrolysis of Ester (I).—Electrolysis was carried out as described above, the current density at the anode being almost identical in value with that employed for the ester (II). The time required was, however, considerably greater. The neutral oil isolated from the product was separated into fractions of b. p. (*a*) below 60°/15 mm., (*b*) 60—80°/15 mm., (*c*) 120°/15 mm., and (*d*) above 120°/15 mm. On hydrolysis with aqueous-alcoholic potash the fraction (*a*) yielded only ββ-dimethylacrylic acid, and (*b*) after redistillation at atmospheric pressure (b. p. 174—176°) yielded a mixture of *as*-dimethylsuccinic acid and a syrupy acid. Owing to the extreme difficulty of separating all the dimethylsuccinic acid from the syrupy acid, the identity of the latter is uncertain. It corresponded in composition and basicity approximately with *methoxypivalic acid* and, on treatment with hydriodic acid, it yielded an acid, m. p. 112—115°, contaminated with a trace of dimethylsuccinic acid. After removal of the latter, as far as possible, the acid agreed approximately in composition and basicity with *hydroxypivalic acid* (m. p. 124°). Hydrolysis of (*c*) yielded a mixture of the methoxy acid and dimethylsuccinic acid.

αα′α′-Tetramethyladipic Acid.—The high-boiling fraction (*d*) yielded, on prolonged hydrolysis with 10 times its volume of concentrated hydrochloric acid, large, colourless, hard crystals, m. p. 191°, which were deposited in the boiling solution. These were almost insoluble in cold and only slightly soluble in boiling water. In organic solvents this acid was much less soluble than its isomeride [Found : C, 59·1; H, 8·85; *M* (dibasic), 203. $C_{10}H_{18}O_4$ requires C, 59·4; H, 8·9%; *M*, 202]. The acid was saturated and, after prolonged heating of its acid chloride with bromine, yielded a bromine-free ester hydrolysable to the original acid.

The authors desire to record their indebtedness to the Government Grant Committee of the Royal Society (E. H. F.) and to the Chemical Society (J. K.) for grants towards the cost of materials.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
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CCCVIII.—*The Formation of Phosphinic Acids from Triarylmethoxyphosphorus Dichlorides.*

By DAVID RUNCIMAN BOYD and FREDERICK JAMES SMITH.

THE tendency of tervalent phosphorus to acquire a higher valency is strikingly exhibited in the conversion of triphenylmethoxyphosphorus dichloride into triphenylmethylphosphinic acid (Boyd and Smith, J., 1924, **125**, 1477):

$$CPh_3\cdot O\cdot P^{III}Cl_2 \xrightarrow{\text{alc. KOH}} CPh_3\cdot P^{V}O(OEt)(OK).$$

Hydrolysis of the phosphorus chloride is in this case accompanied by a molecular rearrangement involving the transference of the triphenylmethyl radical from oxygen to phosphorus. The hydrolytic decomposition of alkyloxyphosphorus dichlorides usually proceeds, however, on quite different lines, no migration of the alkyl group taking place:

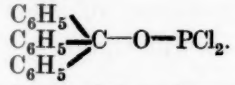
$$RO\cdot P^{V}HO(OH) \xleftarrow{H_2O} RO\cdot P^{III}Cl_2 \xrightarrow{H_2O} ROH + HP^{V}O(OH)_2$$

In view of the unusual behaviour of the phosphorus chloride derived from triphenylcarbinol it has been thought desirable to investigate the action of hydrolysing agents upon a variety of triarylmethoxyphosphorus dichlorides. The interesting observations of Olivier (*Rec. trav. chim.*, 1922, **41**, 301) and of Lapworth and Shoesmith (J., 1922, **121**, 1391) have shown how greatly the ease of hydrolysis of benzyl halides is affected both by the chemical nature and by the orientation of substituents, and it seemed probable that similar phenomena would be met with in the behaviour of substituted triphenylmethoxyphosphorus chlorides towards hydrolysing agents. The present communication deals with the following compounds:

(I.) (*p*) $X\cdot C_6H_4\cdot CPh_2\cdot O\cdot PCl_2$ (X = NO_2, Cl, Br, Me, or OMe)
(II.) (*m*) $OMe\cdot C_6H_4\cdot CPh_2\cdot O\cdot PCl_2$
(III.) (α and β) $C_{10}H_7\cdot CPh_2\cdot O\cdot PCl_2$.

The parent substance of this group, triphenylmethoxyphosphorus dichloride, is characterised by two peculiarities: (i) its extraordinary stability towards water and aqueous alkalis, (ii) the smoothness with which it undergoes rearrangement to a phosphinic acid under the influence of hot alcoholic potash. In a previous paper, it was

suggested that the first step in the hydrolysis of a substance of the type $RO{\cdot}PCl_2$ is the formation of the compound $RO{\cdot}PHCl_2{\cdot}OH$ by addition of the elements of water. On this view the stability towards aqueous alkalis which is shown by the $-PCl_2$ group in triphenylmethoxyphosphorus dichloride may be attributed to a diminution in the free affinity of the phosphorus atom resulting from the enhanced valency demand of the oxygen:



On the other hand, the ability of the substance to undergo molecular rearrangement under the influence of alcoholic potash is—it can scarcely be doubted—connected with the capacity for independent existence which is possessed by the radicals $-CAr_3$, and which is exhibited in greater or less degree in the dissociation of the hexarylethanes.

Intimately related to this capacity for independent existence on the part of the radicals $-CAr_3$ is the basic character which distinguishes the triarylcarbinols. Measurements of the "basicities" of the different carbinols have therefore been carried out by the method of Baeyer and Villiger (*Ber.*, 1902, **35**, 3020) and the figures obtained are included in the following table, in which the most important properties of the triarylmethoxyphosphorus dichlorides are summarised.

			Properties of $R{\cdot}O{\cdot}PCl_2$.	
Radical.	Basicity of carbinol.	% Yield of phosphinic acid as by-product in preparation of $R{\cdot}O{\cdot}PCl_2$.	Behaviour towards hot aqueous ammonia.	% Yield of phosphinic acid on treatment with alc. KOH.
p-Nitrotriphenylmethyl	0·76		Stable.	*
p-Chlorotriphenylmethyl	0·79	4·7	,,	93
p-Bromotriphenylmethyl	0·89	4·9	,,	90
Triphenylmethyl	1	5	,,	91
m-Anisyldiphenylmethyl	1·28	4·1	,,	80
β-Naphthyldiphenylmethyl	2·04	5·3	,,	77
p-Tolyldiphenylmethyl...	2·56 (2·55)*B*	6·7	,,	75
p-Anisyldiphenylmethyl	6·5 (6·99)*B* (6·3)*A*	9·5	Slowly hydrolysed to carbinol.	Nil.
α-Naphthyldiphenylmethyl	8·0 (8·83)*B*	10·75	Stable.	,,

A, Baeyer and Villiger, *Ber.*, 1902, **35**, 3020. *B*, Skraup and Freundlich, *Ber.*, 1922, **55**, 1073.

* Reduction of the nitro-group caused difficulty in this case. An organic acid containing phosphorus was formed, but it was not possible to isolate it in a pure state.

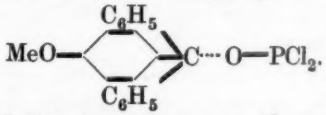
Discussion of Results.

(1) The figures in the last column of the table can only be regarded as approximate values, but they point to the conclusion that a close relationship exists between the "basicities" of the carbinols and the capacities of their phosphorus chlorides to give rise to phosphinic acids under the influence of alcoholic potash. It would appear that there is an optimum position corresponding with a basicity of about 0·75, and that increase of basicity above this figure tends to diminish the yield of phosphinic acid produced by the action of alcoholic potassium hydroxide. If the basicity figures be taken as giving a measure of the dissociating tendencies of the radicals $-CAr_3$, it may be concluded that, whilst a certain degree of dissociating power on the part of the radical is necessary if a molecular rearrangement of this nature is to take place at all, any increase above this minimum value militates against a simple migration of the $-CAr_3$ group from oxygen to phosphorus. Greater dissociating power implies greater stability on the part of the free radical, and this will tend to increase its chances of passing out of the sphere of influence of the phosphorus atom. The molecular rearrangement is conveniently represented by the electronic equation :

$$Ar_3C{:}\dot{O}{:}P{:}X \rightleftharpoons Ar_3C^{+} + {:}\dot{O}{:}P{:}X^{-} = {:}\dot{O}{:}P_{+}{:}X^{-CAr_3}$$

At present there is no evidence to show whether the migration occurs before or after the exchange of Cl for OEt.

(2) Of the phosphorus chlorides investigated, the only one which does not resist prolonged treatment with hot aqueous ammonia is that derived from *p*-anisyldiphenylcarbinol. This fact appears, at first sight, to contradict the view previously developed with regard to the hydrolysis of compounds of the type $R{\cdot}O{\cdot}PCl_2$, according to which the stability of the PCl_2 group in the *p*-anisyl derivative should be greater than that of the same group in the parent substance :



In a molecule of this type, however, there are two points at which hydrolytic attack may occur : .

(i) $RO{\cdot}PCl_2 \xrightarrow[H_2O]{} RO{\cdot}P(OH)(Cl_2)H \xrightarrow[H_2O]{-HCl} RO{\cdot}P(=O)(H)OH$

(ii) $R|O{\cdot}PCl_2 \xrightarrow[H_2O]{} R{\cdot}OH + HO{\cdot}PCl_2 \longrightarrow R{\cdot}OH + HO{\cdot}P(=O)(H)OH$;

and since the products obtained by the action of hot aqueous ammonia upon *p*-anisyldiphenylmethoxyphosphorus dichloride are the carbinol and phosphorous acid, it is not illegitimate to conclude that hydrolysis occurs according to scheme (ii). That a *para*-placed methoxyl group should increase the ease of hydrolytic fission at the linking R—O is in agreement with general experience (compare Lapworth and Shoesmith, *loc. cit.*).

The absence of instability in the parallel case of the phosphorus dichloride derived from α-naphthyldiphenylcarbinol may be attributed to the steric hindrance which the naphthyl group will offer to the process of hydrolysis.

(3) It has already been suggested (*loc. cit.*) that the reaction between phosphorus trichloride and an alcohol usually proceeds according to the following scheme:

$$\text{(i)}\quad \text{RO}|\text{H} + \text{PCl}_3 = \text{RO}\cdot\text{PHCl}_3 = \text{RO}\cdot\text{PCl}_2 + \text{HCl};$$

but that in cases where the alcohol has pronounced basic properties and, therefore, some tendency to dissociate into R and OH, reaction may also take place as follows:

$$\text{(ii)}\quad \text{R}|\text{OH} + \text{PCl}_3 = \text{R}\cdot\text{P(OH)Cl}_3 = \text{R}\cdot\text{POCl}_2 + \text{HCl}.$$

This assumption makes it possible to account in a simple fashion for the presence of $Ph_3C\cdot PO(OH)_2$ amongst the by-products of the reaction between PCl_3 and $Ph_3C\cdot OH$. From this hypothesis it may be deduced that the yield of phosphinic acid obtainable as a by-product in the reaction between $R\cdot OH$ and PCl_3 will be the larger the greater the "basicity" of the alcohol employed. The figures recorded in column 2 (p. 2324) show that the yields of phosphinic acid obtained from the different triarylcarbinols in the course of this investigation are in substantial agreement with this deduction.

Experimental.

In the preparation of the triarylmethoxyphosphorus dichlorides, the carbinol (1 mol.) was slowly added to phosphorus trichloride (about 2 mols.) cooled in ice, and the reaction mixture kept at least 48 hours at room temperature. The resulting solid was treated with ice and water, digested in the cold, during several days, first with ammonia and afterwards with sodium carbonate solution, washed free from alkali, dried in a vacuum, and crystallised from a suitable solvent. On acidification of the alkaline filtrate, a small quantity of triarylmethylphosphinic acid was precipitated; but in order to obtain the maximum yield of phosphinic acid, formed as a by-product in the preparation of a triarylmethoxyphosphorus dichloride, it was usually necessary to carry out the digestion with ammonia on the steam-bath.

The triarylmethoxyphosphorus dichlorides all dissolve in cold concentrated sulphuric acid with evolution of hydrogen chloride, and from the strongly coloured solutions the carbinols are precipitated on addition of water.

For the conversion of a triarylmethoxyphosphorus dichloride into a triarylmethylphosphinic acid, the chloride (1 mol.) was heated in a water-bath with potassium hydroxide (4·5—5 mols.) and ethyl alcohol (about 99% Et·OH). Heating was continued for a short time after potassium chloride had separated and then water was added and the alcohol evaporated on the steam-bath. The aqueous solution was boiled for some time and, when cold, was filtered from undissolved material and strongly acidified with hydrochloric acid. The precipitated mono-ethyl ester of the triarylmethylphosphinic acid was refluxed for an hour with glacial acetic acid–concentrated hydriodic acid. From this solution the phosphinic acid separated on cooling: the crystals were washed, and weighed after drying at 110°. A further small quantity of acid was obtained on addition of water to the filtrate. This was collected and included in the yield. From 5 g. of triphenylmethoxyphosphorus dichloride, 3·8 g. of potassium hydroxide, and 38 c.c. of alcohol, the yield of triphenylmethylphosphinic acid was 4·079 g. or 91% of the theoretical.

The acids obtained by this molecular rearrangement are all dibasic, in agreement with the constitutional formula which has been assigned, $CAr_3 \cdot PO(OH)_2$. The basicity was established by the preparation of the corresponding dipotassium salts and by electrometric titration.

p-*Chlorotriphenylmethoxyphosphorus Dichloride* (I; X = Cl).—The carbinol required was prepared by the Grignard reaction from ethyl *p*-chlorobenzoate. The crude product (after steam distillation to remove unchanged ester, etc.) was kept for some days; the main portion then became crystalline. The crystals were finely powdered, washed with cold light petroleum, and crystallised from petroleum (b. p. 80—100°); they then melted at 85°, in agreement with the figure given by Gomberg and Cone (*Ber.*, 1906, **39**, 3278), who prepared the compound from *p*-chlorobenzophenone dichloride. The yield was about 35% of the theoretical.

The pure p-*chlorotriphenylmethoxyphosphorus dichloride* was obtained from the crude chloride by dissolution in chloroform and addition of an equal volume of acetone. It formed minute, colourless crystals, m. p. 161·5° (Found: P, 7·8; Cl, 26·9. $C_{19}H_{14}OCl_3P$ requires P, 7·85; Cl, 26·9%).

The dichloride was moderately easily soluble in boiling ethyl alcohol, but on refluxing for an hour it decomposed with formation of the carbinol and a trace of oil which was not identified. Heating

with an alcoholic solution of potassium hydroxide brought about an almost quantitative conversion into *p*-chlorotriphenylmethylphosphinic acid: from 4·6 g. of the phosphorus dichloride, 3·5 g. of potassium hydroxide, and 48 c.c. of alcohol, the yield of phosphinic acid was 3·9 g. or 93% of the theoretical. The sticky by-product (0·14 g.), insoluble in alkali, separated from benzene and light petroleum in colourless crystals, m. p. 146°; it was not identified.

p-*Chlorotriphenylmethylphosphinic acid*, $C_6H_4Cl\cdot CPh_2\cdot PO(OH)_2$, crystallises from acetic acid or benzene in minute crystals, m. p. 273° (Found in material kept in a vacuum desiccator for some days: P, 8·8; Cl, 9·85. $C_{19}H_{16}O_3ClP$ requires P, 8·7; Cl, 9·9%).

The *dipotassium* salt, prepared by dissolving the acid in boiling concentrated potassium hydroxide solution, separated in small, lustrous plates. These were washed with absolute alcohol and air-dried (Found: K, 13·6; H_2O, 24·75. $C_{19}H_{14}O_3ClPK_2,8H_2O$ requires K, 13·5; H_2O, 24·8%).

p-*Bromotriphenylmethoxyphosphorus Dichloride* (I; X = Br).—The carbinol was prepared from ethyl *p*-bromobenzoate, and purified by the method of Gomberg and Blicke (*J. Amer. Chem. Soc.*, 1923, **45**, 1770), *viz.*, conversion into the chloride by hydrogen chloride in dry ethereal solution, followed by hydrolysis with aqueous acetone in presence of dimethylaniline. The product melted at 82°, even after repeated crystallisation from benzene and light petroleum (Gomberg and Blicke give m. p. 130°). A specimen of the carbinol purified by recrystallisation of the crude substance melted at 78°, as recorded by Gomberg and Cone (*Ber.*, 1906, **39**, 3279).

p-*Bromotriphenylmethoxyphosphorus dichloride* crystallises from benzene or chloroform–acetone in small, colourless crystals, m. p. 163° (Found: P, 7·3; Cl, 16·1. $C_{19}H_{14}OCl_2BrP$ requires P, 7·05; Cl, 16·1%). In properties it closely resembles the corresponding *p*-chloro-compound.

p-*Bromotriphenylmethylphosphinic Acid*, $C_6H_4Br\cdot CPh_2\cdot PO(OH)_2$.—From 5 g. of the phosphorus dichloride, with 3·18 g. of potassium hydroxide and 32 c.c. of alcohol, the yield of phosphinic acid was 4·15 g. (90%). The acid dissolves readily in boiling benzene, alcohol, or glacial acetic acid. From acetic acid, it separates in small, colourless crystals, m. p. 297°, containing a molecule of acetic acid, which is retained after prolonged keeping in a vacuum, but may be driven off by heating for several hours at 100° (Found: $CH_3\cdot CO_2H$, 13·0. $C_{19}H_{16}O_3BrP,CH_3\cdot CO_2H$ requires $CH_3\cdot CO_2H$, 13·0%. Found in material heated at 100°: P, 7·9; Br, 19·8. $C_{19}H_{16}O_3BrP$ requires P, 7·7; Br, 19·85%).

The *dipotassium* salt forms glistening plates (Found: K, 12·6; P, 5·2; H_2O, 20·25. $C_{19}H_{14}O_3BrPK_2,7H_2O$ requires K, 12·9;

P, 5·1; H_2O, 20·8%). The *barium* salt was obtained as a heavy, white precipitate from barium chloride and the potassium salt in aqueous solution (Found: Ba, 21·9; H_2O, 14·8.

$$C_{19}H_{14}O_3BrPBa,5H_2O$$

requires Ba, 21·8; H_2O, 14·3%).

Diphenyl-p-*anisylmethoxyphosphorus Dichloride* (I; X = OMe).—The carbinol was prepared from ethyl *p*-anisate. Crystallisation from ether–ligroin as recommended by Baeyer and Villiger (*Ber.*, 1902, **35**, 3027) was not found satisfactory. A fair yield of pure subtance was obtained by submitting the oily carbinol, left after steam distillation, to distillation under reduced pressure (b. p. 247°/18 mm.). The glassy solid so obtained was dissolved in ether–light petroleum, the solvent removed in a vacuum, and the yellow, crystalline residue ground with light petroleum, which removed a small quantity of oily impurity leaving a white, crystalline product, m. p. 84° (yield 30%).

The carbinol reacts readily with phosphorus trichloride giving an orange-coloured solid. The crude diphenyl-*p*-anisylmethoxyphosphorus dichloride, after treatment with water and alkalis, was digested with cold ether for some hours, and then repeatedly crystallised from much benzene–light petroleum, which was heated as little as possible. It was finally obtained in minute, white crystals, m. p. 180° (Found: P, 7·8; Cl, 17·9. $C_{20}H_{17}O_2Cl_2P$ requires P, 7·9; Cl, 18·2%).

In one experiment 13 g. of the carbinol gave 11 g. of crude chloride, and from the alkaline filtrates, on acidification, 1·5 g. of *diphenyl*-p-*anisylmethylphosphinic acid* were precipitated, m. p. 210° after crystallisation from acetic acid. This acid is not decomposed on boiling with concentrated potassium hydroxide solution. Diphenyl-*p*-anisylmethoxyphosphorus dichloride shows a high degree of stability towards cold aqueous alkalis, but on digestion on the water-bath for 6 hours with aqueous ammonia it is decomposed to the carbinol and phosphorous acid. Treatment with hot alcoholic potassium hydroxide, carried out in the usual way, yielded, not the phosphinic acid, but a sticky solid which became brittle on keeping for some weeks. On crystallisation from petroleum (b. p. 60—80°), it yielded (along with a small quantity of yellow oil) colourless crystals, m. p. 82°. These were identified as diphenyl-*p*-anisylcarbinol by a mixed melting point determination, and by conversion into the carbinol chloride, m. p. 124°.

Diphenyl-m-*anisylmethoxyphosphorus Dichloride* (II).—The carbinol, prepared from ethyl *m*-anisate (Baeyer, von Bentheim, and Diehl, *Annalen*, 1907, **354**, 152), formed transparent prisms, m. p. 90·5°. The crude phosphorus dichloride is readily soluble in ether.

Separation from unchanged carbinol or carbinol chloride is conveniently effected by crystallisation from acetone–chloroform. The pure substance forms minute, snow-white crystals, m. p. 122—124° (Found: P, 7·85; Cl, 18·15. Calc. for $C_{20}H_{17}O_2Cl_2P$: P, 7·9; Cl, 18·2%).

The chloride dissolved slowly in boiling absolute alcohol. The crystals which separated on evaporation of the alcoholic solution were identified as the carbinol by a mixed melting point.

The dichloride (38 g.), heated with 28 g. of potassium hydroxide and 250 c.c. of alcohol, gave 30 g. of crude monoethyl phosphinic ester (P, 8·0%) (yield 80%). It was not possible to isolate the diphenyl-*m*-anisylmethylphosphinic acid. Boiling the ethyl ester with acetic acid–hydriodic acid converted it into m-*hydroxytriphenylmethylphosphinic acid*, $HO{\cdot}C_6H_4{\cdot}CPh_2{\cdot}PO(OH)_2$, fine, white needles which shrink at 239° and melt at 248°. The hydroxy-acid is very soluble in acetic acid and in cold alcohol. Even after crystallisation from glacial acetic acid and drying in a vacuum the substance was associated with 2 mols. of water, which were lost on drying at 100° (Found: H_2O, 9·3. $C_{19}H_{17}O_4P,2H_2O$ requires H_2O, 9·6%. Found for the anhydrous acid: C, 67·1; H, 5·35; P, 9·3, 9·1. $C_{19}H_{17}O_4P$ requires C, 67·05; H, 5·0; P, 9·1%).

The *disodium* salt, $HO{\cdot}C_6H_4{\cdot}CPh_2{\cdot}PO(ONa)_2$, formed lustrous plates which were dried at 100° (Found: P, 8·2; Na, 11·4. $C_{19}H_{15}O_4PNa_2$ requires P, 8·1; Na, 11·3%).

On benzoylating the hydroxy-acid by the Schotten-Baumann method the sodium salt of the *benzoyl* derivative separated as a white powder. The acid, prepared from this salt, crystallised from alcohol on addition of light petroleum in minute, white crystals, m. p. 237·5°, which were dried at 100° (Found: C, 70·05; H, 5·0; P, 7·0. $C_{26}H_{21}O_5P$ requires C, 70·3; H, 4·8; P, 7·0%). The *disilver* salt of the benzoylated acid was obtained as a white precipitate on adding silver nitrate to a solution of the acid in ammonia (Found, in material dried in a vacuum: H_2O, 5·65; Ag, 31·2. $C_{26}H_{19}O_5PAg_2,2H_2O$ requires H_2O, 5·2; Ag, 31·1%).

m-Hydroxytriphenylmethylphosphinic acid, on methylation with methyl sulphate, gave an *acid* which, after recrystallisation from glacial acetic acid, melted at 197°, and behaved as a dibasic acid on titration (Found: C, 67·5; H, 5·7; P, 8·65. $C_{20}H_{19}O_4P$ requires C, 67·8; H, 5·5; P, 8·8%).

Diphenyl-α-naphthylmethoxyphosphorus Dichloride (III).—The carbinol, prepared by the method of Acree (*Ber.*, 1904, **37**, 627), after repeated crystallisation from benzene–ligroin, formed almost colourless crystals, m. p. 136·5°. The crude *phosphorus dichloride* was digested with ether, triturated with cold acetone, and recrystal-

lised from benzene–ligroin. It formed white, microscopic crystals, m. p. 171—172° (Found : P, 7·65, 7·4; Cl, 17·2. $C_{23}H_{17}OCl_2P$ requires P, 7·5; Cl, 17·3%).

The pure chloride is insoluble in cold ether, acetone, or light petroleum, but dissolves readily in warm benzene. It dissolves slowly in boiling absolute alcohol, and the solution, on cooling, deposits crystals of the ethyl ether of diphenyl-α-naphthylcarbinol, m. p. 134° (Found : C, 88·5; H, 6·6. Calc. for $C_{25}H_{22}O$: C, 88·8; H, 6·5%).

On treatment with potassium hydroxide and alcohol according to the usual method the phosphorus dichloride was converted into the carbinol (identified by the mixed melting point method and by reduction to diphenyl-α-naphthylmethane), and no phosphinic acid was produced.

Diphenyl-α-naphthylmethylphosphinic acid, $C_{10}H_7 \cdot CPh_2 \cdot PO(OH)_2$, was obtained as a by-product in the preparation of diphenyl-α-naphthylmethoxyphosphorus dichloride. In one experiment using 10 g. of carbinol, the yield of phosphinic acid obtained on acidifying the alkaline filtrates was 1·3 g. (10·8%). After recrystallisation from alcohol it formed fine needles, m. p. 256°, which were dried at 100° (Found : P, 8·1; C, 73·6; H, 5·2. $C_{23}H_{19}O_3P$ requires P, 8·3; C, 73·8; H, 5·1%).

Dipotassium diphenyl-α-naphthylmethylphosphinate separates in lustrous plates on cooling a solution of the acid in hot concentrated potash (Found : H_2O, 16·1; K, 14·3. $C_{23}H_{17}O_3PK_2,5H_2O$ requires H_2O, 16·7; K, 14·4%).

Diphenyl-β-naphthylmethoxyphosphorus Dichloride (III).—The carbinol, m. p. 118°, was obtained in excellent yield from β-naphthoic ester by the method of Gomberg and Sullivan (*J. Amer. Chem. Soc.*, 1922, **44**, 1810). The crude phosphorus dichloride was digested with ether and crystallised from chloroform–acetone, small, white crystals, m. p. 194°, being obtained (Found : P, 7·65; Cl, 17·4. $C_{23}H_{17}OCl_2P$ requires P, 7·5; Cl, 17·3%).

Boiling with absolute alcohol converts it into the ethyl ether of diphenyl-β-naphthylcarbinol, m. p. 116°. On treating 5 g. of diphenyl-β-naphthylmethoxyphosphorus dichloride with 3·41 g. of potassium hydroxide and 34 c.c. of alcohol, the yield of *diphenyl-β-naphthylmethylphosphinic acid*, $C_{10}H_7 \cdot CPh_2 \cdot PO(OH)_2$, was 3·5 g. (77%). After recrystallisation the acid formed colourless needles, m. p. 247·5°. The crystals from acetic acid contain one molecule of solvent. The sample analysed had been kept for a week in a vacuum over lime (Found : $CH_3 \cdot CO_2H$, 13·8; P, 8·3; C, 73·45; H, 5·1. $C_{23}H_{19}O_3P,CH_3 \cdot CO_2H$ requires $CH_3 \cdot CO_2H$, 13·8; P, 8·3; C, 73·8; H, 5·1%).

From the acid, a *dipotassium* salt was prepared (Found: H_2O, 17·0; P, 5·8; K, 14·3. $C_{23}H_{17}O_3PK_2,5H_2O$ requires H_2O, 16·7; P, 5·7; K, 14·4%).

The oily by-product formed in the treatment of the phosphorus dichloride with alcoholic potash was crystallised from ether–light petroleum and identified as the ethyl ether of diphenyl-β-naphthylcarbinol.

p-*Nitrotriphenylmethoxyphosphorus Dichloride* (I; X = NO_2).—The carbinol, m. p. 98°, was prepared by a Friedel-Crafts reaction from *p*-nitrobenzophenone dichloride (Baeyer and Villiger, *Ber.*, 1904, **37**, 606). The yield was poor, much of the nitroketone being recovered.

The crude *phosphorus dichloride* was dissolved in warm benzene, and a small quantity of light petroleum added; a red solid was then thrown down. The filtered solution deposited clear yellow crystals. By dissolving these in the least possible volume of chloroform and adding about twice the bulk of acetone, colourless crystals were finally obtained, m. p. 188·5° (Found: P, 7·7; Cl, 17·55. $C_{19}H_{14}O_3NCl_2P$ requires P, 7·65; Cl, 17·5%).

The chloride is difficultly soluble in boiling absolute alcohol and crystallises unchanged even after refluxing for an hour. On treatment with alcoholic potassium hydroxide an acid containing phosphorus and nitrogen was obtained. It was very dark in colour and attempts to crystallise it failed.

Diphenyl-p-*tolylmethoxyphosphorus Dichloride* (I; X = Me).—[With Mr. J. D. Tully.] The carbinol was prepared by the Grignard reaction from benzophenone (Acree, *Ber.*, 1904, **37**, 992). Crystallised from ligroin, the substance melted at 78° (Acree gives 74°); but the crystals obtained from benzene melted at 73—74°.

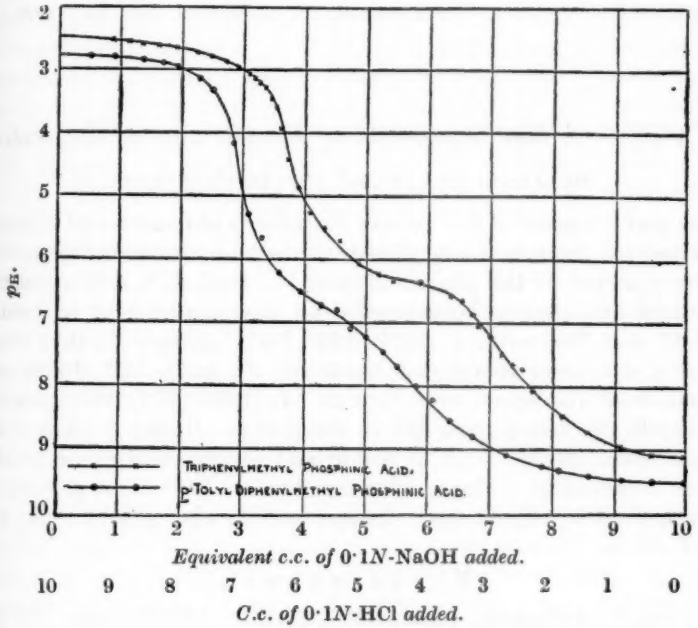
The carbinol and phosphorus trichloride were mixed in the cold as in previous cases, but the reaction was completed by heating for 2 hours at 40—50°. The crude chloride, after being extracted twice with ether, crystallised from benzene in minute, colourless crystals, m. p. 193° (decomposition) (Found: P, 8·4; Cl, 18·65. $C_{20}H_{17}OCl_2P$ requires P, 8·3; Cl, 18·9%).

The phosphorus dichloride dissolves in boiling absolute alcohol, and the solution, on cooling, deposits crystals of the carbinol (Found: C, 87·4; H, 6·7. Calc. for $C_{20}H_{18}O$: C, 87·5; H, 6·6%).

Diphenyl-p-*tolylmethylphosphinic Acid*, $C_6H_4Me{\cdot}CPh_2{\cdot}PO(OH)_2$.—From 5 g. of the phosphorus dichloride, with 3·74 g. of potassium hydroxide and 37·4 c.c. of alcohol, the yield of phosphinic acid was 3·4 g. (75%). After treatment with acetic acid–hydriodic acid and crystallisation from benzene, the phosphinic acid melted at 254°. The crystals contained one molecule of water, which was removed

on heating at 100° for some hours (Found : H_2O, 5·6; C, 67·4, 67·7; H, 6·0, 5·9; P, 8·9, 8·4. $C_{20}H_{19}O_3P,H_2O$ requires H_2O, 5·1; C, 67·4; H, 5·9; P, 8·7%). On recrystallisation from glacial acetic acid the water molecule is replaced by a molecule of acetic acid (Found : $CH_3{\cdot}CO_2H$, 15·5. $C_{20}H_{19}O_3P,CH_3{\cdot}CO_2H$ requires $CH_3{\cdot}CO_2H$, 15·1%. Found in material heated for some hours at 100° : C, 70·7; H, 5·85; P, 9·4, 9·1. $C_{20}H_{19}O_3P$ requires C, 71·0; H, 5·6; P, 9·2%).

FIG. 1.



The *dipotassium* salt forms pearly leaflets (Found : H_2O, 20·6; K, 14·8; P, 5·9. $C_{20}H_{17}O_3PK_2,6H_2O$ requires H_2O, 20·7; K, 14·9; P, 5·9%).

Electrometric Titration of the Phosphinic Acids.

Owing to the low solubility of the acids in water, it was not practicable to titrate an aqueous solution of the acid with caustic soda. The plan adopted was to dissolve a weighed quantity of acid in excess of standard sodium hydroxide, and back-titrate with standard hydrochloric acid. For the titrations a Rideal hydrogen electrode and a Rideal *N*/10-calomel half-cell were used, the temperature being maintained at 18° throughout the series. Carbonate-

free sodium hydroxide was prepared by the method of Cornog (*J. Amer. Chem. Soc.*, 1921, **43**, 2573) and standardised with acid potassium phthalate.

The titration curves for triphenylmethylphosphinic acid and for diphenyl-*p*-tolylmethylphosphinic acid are given in illustration of the results obtained.

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UNIVERSITY COLLEGE, SOUTHAMPTON. [*Received, June 10th*, 1926.]

CCCIX.—*A New Synthesis of Fisetin and of Quercetin.*

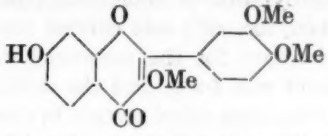
By JAMES ALLAN and ROBERT ROBINSON.

THE first examples of the " direct " synthesis of flavone and flavonol derivatives by aroylation of substituted *o*-hydroxyacetophenones were reported by the present authors (J., 1924, **125**, 2192), and the method has already been applied to the syntheses of myricetin (Kalff and Robinson, J, 1925, **127**, 181), galangin methyl ether (*ibid.*), datiscetin (Kalff and Robinson, J., 1925, **127**, 1968) and kaempferol (Robinson and Shinoda, J., 1925, **127**, 1973) among naturally occurring members of the group. In the present communication the synthesis of fisetin and of quercetin along similar lines is described. These colouring matters have been previously synthesised by Kostanecki, Lampe and Tambor (*Ber.*, 1904, **37**, 784, 1402).

EXPERIMENTAL.

Veratric Anhydride, $[C_6H_3(OMe)_2{\cdot}CO]_2O$.—(A) Pyridine (35 g.) was added to a solution of veratroyl chloride (24 g.) in ether (180 c.c.) and after 2·5 hours small pieces of ice were added. A certain amount of the anhydride crystallised from the solution and was collected. The separated ethereal layer was washed with dilute hydrochloric acid, dried, and evaporated (yield, 16 g.). The substance crystallises from benzene or from ethyl acetate in rectangular prisms, m. p. 124—125° (Found: C, 62·5; H, 5·3. $C_{18}H_{18}O_7$ requires C, 62·4; H, 5·2%). (B) A 20% solution (50 c.c.) of carbonyl chloride in benzene was added to a stirred, ice-cooled mixture of veratric acid (33 g.), pyridine (15 g.) and benzene (50 c.c.). After 2 hours, ice and dilute hydrochloric acid were introduced and the benzene solution was separated, dried and evaporated (yield 75—80%).

7-Hydroxy-3 : 3′ : 4′-trimethoxyflavone (*Fisetin Trimethyl Ether*),



—A mixture of ω-methoxyresacetophenone (2·5 g.) (Slater and Stephen, J., 1920, **117**, 314), veratric anhydride (24 g.) and potassium veratrate (10 g.) was heated for 4·5 hours in an oil-bath at 175—180°. Alcohol (150 c.c.) was added and the solution boiled for 15 minutes, then mixed with potassium hydroxide (8 g.) dissolved in water (25 c.c.) and the alcohol removed by distillation. Carbon dioxide was passed through the filtered solution of the residue in water until no further precipitation occurred. The solid (3·2 g.) crystallised from ethyl acetate (charcoal) in almost colourless needles, m. p. 220° (Found : C, 66·1; H, 4·8. $C_{18}H_{16}O_6$ requires C, 65·9; H, 4·9%). The substance does not develop a coloration with ferric chloride in alcoholic solution and its yellow solution in sulphuric acid exhibits a weak green fluorescence. The *acetyl* derivative, obtained by treatment with boiling acetic anhydride for 2 hours, crystallised from alcohol in colourless needles, m. p. 229° (Found : C, 65·1; H, 5·0. $C_{20}H_{18}O_7$ requires C, 64·9; H, 4·9%). On hydrolysis with aqueous-alcoholic sodium hydroxide fisetin trimethyl ether was easily regenerated.

3 : 7 : 3′ : 4′-Tetramethoxyflavone.—Methyl sulphate (8 c.c.) was gradually added with shaking to a solution of fisetin trimethyl ether (0·7 g.) in water (25 c.c.) containing potassium hydroxide (2 g.). Finally, the solution was rendered strongly alkaline and the precipitated solid (0·7 g.) was collected and crystallised from ethyl acetate in prismatic needles, m. p. 150° (Found : C, 66·3; H, 5·3. Calc. for $C_{19}H_{18}O_6$: C, 66·7; H, 5·3%). This compound has the properties of fisetin tetramethyl ether which is stated by Schmid (*Ber.*, 1886, **19**, 1746) to melt at 152°.

3 : 7 : 3′ : 4′-Tetra-acetoxyflavone (*Tetra-acetylfisetin*).—7-Acetoxy-3 : 3′ : 4′-trimethoxyflavone was converted into fisetin in 35 minutes, by boiling hydriodic acid (*d* 1·7). The yellow solid obtained on the addition of sulphurous acid exhibited the reactions and properties of fisetin, but, as this substance has m. p. (decomp.) above 360°, it was identified by the preparation of the tetra-acetyl derivative in the usual manner. This crystallised from alcohol in colourless needles, m. p. 196—198° (Found : C, 60·4; H, 4·3. Calc. for $C_{23}H_{18}O_{10}$: C, 60·8; H, 4·0%). Tetra-acetylfisetin is stated by A. G. Perkin (J., 1897, **71**, 1195) to melt at 196—198°.

5 : 7-*Dihydroxy*-3 : 3′ : 4′-*trimethoxyflavone* (*Quercetin Trimethyl Ether*).—The veratroylation of ω-methoxyphloracetophenone (3 g.) (Slater and Stephen, *loc. cit.*) was carried out substantially in the manner described above for the resorcinol derivative. The yield of the crude product was 4·9 g. and the substance was crystallised from alcohol and then from ethyl acetate in very pale yellow needles, m. p. 240—245° (Found: C, 62·6; H, 4·5. $C_{18}H_{16}O_7$ requires C, 62·8; H, 4·7%). The addition of ferric chloride to an alcoholic solution produces an intense greenish-brown coloration, and the bright yellow solution in sulphuric acid exhibits a very weak green fluorescence. The *diacetyl* derivative crystallised from alcohol in needles, m. p. 159—160° (Found: C, 61·9; H, 4·5. $C_{22}H_{20}O_9$ requires C, 61·7; H, 4·7%).

3 : 5 : 7 : 3′ : 4′-*Pentamethoxyflavone* (*Quercetin Pentamethyl Ether.*)—The trimethyl ether was methylated by means of methyl sulphate and aqueous potassium hydroxide (compare Waliascko, *Arch. Pharm.*, 1904, **242**, 225, for the similar methylation of quercetin), and the product crystallised from ethyl acetate in needles, m. p. 148°, unaltered by admixture with an authentic specimen prepared from quercetin.

Penta-acetylquercetin.—The quercetin trimethyl ether yielded on demethylation in the usual manner a yellow crystalline product, m. p. 312—316° (decomp.), which exhibited the properties and reactions of quercetin and on acetylation gave a compound crystallising from alcohol in colourless needles, m. p. 191—195°. The m. p. was unaltered by admixture with an authentic specimen of penta-acetylquercetin.

We desire to thank the Department of Scientific and Industrial Research for a grant which has enabled one of us to take part in the research.

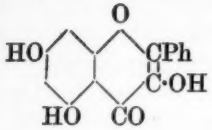
THE UNIVERSITY, MANCHESTER. [*Received, July 3rd,* 1926.]

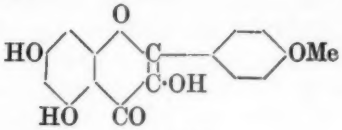
CCCX.—*A Synthesis of Kaempferide and of* iso-*Rhamnetin.*

By TOM HEAP and ROBERT ROBINSON.

THE new direct method of preparation of flavonol derivatives has up to the present been restricted to the synthesis of members of the series which have a methoxyl group situated in position 3 in the pyrone nucleus. We have now devised a modification applicable to the synthesis of 3-hydroxyflavones without demethylation and

have employed the process in the synthesis of galangin (I), kaempferide (II), and *iso*rhamnetin (III).

(I.) 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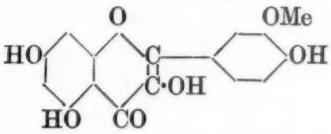
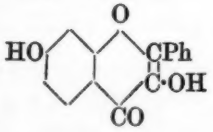
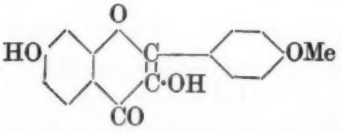
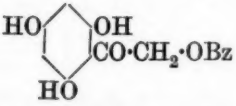
(III.) 

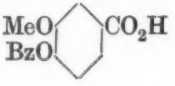
The first experiments were made with resorcinol derivatives and it was found that the protection of hydroxyl groups could be most satisfactorily effected by benzoylation. Ethylcarbonato-derivatives were not found to be sufficiently stable and the use of acetates was prohibited by the experience of Kalff and Robinson (J., 1925, **127**, 1972) who noted that *o*-acetoxybenzoic anhydride as a component in an attempted flavonol synthesis led to the formation of a 2-methylchromone derivative. *ω-Benzoyloxyresacetophenone* (IV) is obtained by a Hoesch reaction from benzoyloxyacetonitrile, $CH_2(OBz)\cdot CN$ (Aloy and Rabaut, *Bull. Soc. chim.*, 1913, **13**, 457), and resorcinol. On benzoylation and anisoylation followed by hydrolysis, resogalangin (V) and resokaempferide (VI) were respectively obtained.

(V.) 


(VI.)

The analogous preparation of *ω-benzoyloxyphloracetophenone* (VII) involved experimental difficulties, but these having been overcome, benzoylation and anisoylation followed by hydrolysis, afforded galangin (I) and kaempferide (II) respectively.

(VII.) 


(VIII.)

The synthetical kaempferide had m. p. 225° and its triacetyl derivative had m. p. 193—194°. Jahns (*Ber.*, 1881, **14**, 2385) was the first to obtain the pure substance from galangal root and assigned the m. p. 221—222°. Ciamician and Silber (*Ber.*, 1899, **32**, 861) gave the m. p. 227—229° for the flavonol, and 193—195° for its triacetate. Testoni (*Gazzetta*, 1900, **30**, ii, 327) stated that the

triacetyl derivative melted at 193—194°. We were unable to obtain a specimen of the natural product but the properties of kaempferide and its derivatives recorded by these authors and by Perkin and Wilson (J., 1903, **83**, 136) are characteristic and were exhibited by the synthetical material. The question of the identity or non-identity of the kaempferol methyl ether, isolated by Oesch and Perkin (J., 1914, **105**, 2350) from *Rhamnus catharticus*, with kaempferide remains an open one. This product had m. p. 221—222° and its acetyl derivative had m. p. 200—201°. The extension of the general process to the synthesis of *iso*rhamnetin was accomplished by the use of benzoylvanillic acid (VIII), the anhydride and sodium salt of which were heated with ω-benzoyloxyphloracetophenone at 180—185°. The product, probably a tetrabenzoyltrivanilloyl *iso*rhamnetin, yields *iso*rhamnetin (III) on hydrolysis. This flavonol was first isolated by Perkin and Hummel (J., 1896, **69**, 1566) from yellow wallflowers and subsequently it was found to be obtainable from asbarg (*Delphinium zalil*) (Perkin and Pilgrim, J., 1898, **73**, 268) and from red clover flowers (Power and Salway, J., 1910, **97**, 245). The m. p. of the tetra-acetyl derivative is given as 195—196° and 198—200°, but the synthetical material has m. p. 205—207°, and there is also a discrepancy in the m. p.'s of the natural and synthetic flavonols. We have, however, succeeded in isolating from yellow wallflower petals a flavonol the acetyl derivative of which has m. p. 205—207° not depressed by admixture with the synthetical specimen.

Experimental.

ω-*Benzoyloxyresacetophenone* (IV).—Hydrogen chloride was passed into an ice-cooled solution of benzoyloxyacetonitrile (7·4 g.) and resorcinol (5·1 g.) in anhydrous ether (30 c.c.) for 5 hours. On the following day the ether was decanted and the hard deposit washed with fresh ether. A further quantity of the solid separated when the ethereal washings were added to the mother-liquor. The ketimine hydrochloride was hydrolysed by heating with water for an hour on the steam-bath when the material did not dissolve but changed completely in appearance. The product (10 g.) was collected, dried at 100°, and crystallised from absolute alcohol (yield 9 g.) in colourless, well-formed plates, m. p. 202—203° (Found: C, 66·4; H, 4·6. $C_{15}H_{12}O_5$ requires C, 66·2; H, 4·4%). The alcoholic solution develops a deep brownish-violet coloration (red in thick layers) on the addition of ferric chloride. The substance is readily soluble in acetone, ethyl acetate and hot alcohol, sparingly soluble in chloroform and benzene, and very sparingly in water, ether, and light petroleum. The *diacetyl* derivative, obtained by

the action during 1 hour of boiling acetic anhydride in presence of a drop of pyridine, crystallised from alcohol in long, lustrous, colourless needles, m. p. 112—113° (Found: C, 63·9; H, 4·7. $C_{19}H_{16}O_7$ requires C, 64·0; H, 4·5%).

3 : 7-*Dihydroxyflavone* (V).—ω-Benzoyloxyresacetophenone (7 g.), benzoic anhydride (15 g.) and sodium benzoate (6 g.) were heated together for 3 hours at 180—185° with mechanical stirring. The cooled product was crushed and added to alcohol (100 c.c.), and a solution of potassium hydroxide (10·3 g.) in water (15 c.c.) was gradually introduced to the heated mixture, which was finally boiled for 30 minutes and then concentrated by distillation of the alcohol. The residue was dissolved in water and the flavonol precipitated by the passage of carbon dioxide as a brown powder (dried, 6·1 g.). The substance was purified by precipitation from an alcoholic solution by water and by repeated crystallisation (charcoal) from methyl alcohol, finally in a mass (2·5 g.) of pale yellow, hair-fine, silky, needles, m. p. 258°, which, air-dried, lost 11·5% at 110° (Found in dried material: C, 70·6; H, 4·2. Calc. for $C_{15}H_{10}O_4$, CH_4O : CH_4O, 11·2%; and for $C_{15}H_{10}O_4$: C, 70·9; H, 3·9%). The substance has been previously obtained by Kostanecki and Stoppani (*Ber.*, 1904, **37**, 1180) and by Robinson and Shinoda (J., 1925, **127**, 1973). The specimen now described melted at 258° when mixed with that of the same m. p. prepared by the last-named authors. The diacetyl derivative crystallised from alcohol in colourless needles, m. p. 157·5—158·5° (Found: C, 67·3; H, 4·3. Calc. for $C_{19}H_{14}O_6$: C, 67·5; H, 4·1%). Kostanecki and Stoppani (*loc. cit.*) give m. p. 157°.

3 : 7-*Dihydroxy*-4′-*methoxyflavone* (VI).—The preparation of this resokaempferide resembled that of resogalangin just described. The starting materials were ω-benzoyloxyresacetophenone (7 g.), anisic anhydride (29 g.) and sodium anisate (7 g.), and hydrolysis was effected by means of alcohol (50 c.c.) and 20% alcoholic potassium hydroxide (152 c.c.). The yield of crude product was 6·2 g.; this was acetylated by boiling for 1 hour with acetic anhydride (20 g.) and a drop of pyridine, and the *diacetyl* derivative crystallised from alcohol (charcoal) as a mass of fine, white, silky needles, m. p. 197° (yield 2·2 g.) (Found: C, 65·1; H, 4·4. $C_{20}H_{16}O_7$ requires C, 65·2; H, 4·3%). The substance was hydrolysed by means of 10% aqueous potassium hydroxide on the steam-bath and the pale yellow 3 : 7-*dihydroxy*-4′-*methoxyflavone* obtained on acidification with hydrochloric acid crystallised from methyl alcohol in glistening, pale yellow leaflets, m. p. 283—284° (Found: C, 67·3; H, 4·4. $C_{16}H_{12}O_5$ requires C, 67·6; H, 4·2%). The substance also crystallises well from acetic acid in clusters of needles and its pale yellow

solutions exhibit a green fluorescence. The lemon-yellow solution in concentrated sulphuric acid exhibits an intense bluish-green fluorescence which is a little greener than that characteristic of kaempferide. On standing, the fluorescence becomes much bluer. An alcoholic solution of the flavonol becomes deep brown on the addition of ferric chloride. The *lead* salt is a lemon-yellow precipitate. On mixing saturated boiling methyl-alcoholic solutions of the flavonol and potassium acetate, a pale yellow *potassium* salt is deposited and this is decomposed on boiling with water (compare A. G. Perkin and Wilson, J., 1903, **83**, 136).

ω-*Benzoyloxyphloracetophenone* (VII).—An ice-cooled solution of benzoyloxyacetonitrile (10 g.) and anhydrous phloroglucinol (8·6 g.) in ether (70 c.c.) was saturated with hydrogen chloride during 5 hours and the mixture allowed to remain in the ice-bath for 12 hours. The ketimine hydrochloride was deposited as a pale yellow crust and was collected and washed with ether. Many unsuccessful experiments were made before it was found that the hydrolysis of the salt could be conveniently effected by boiling with 50% aqueous alcohol (200 c.c.) for 21 hours under reflux. Most of the alcohol was removed by distillation and the material which crystallised on cooling was collected, washed with boiling water and dried (11 g.). A further quantity (2·5 g.) was recovered from the mother-liquor and one crystallisation of the whole crude product from aqueous alcohol gave 12 g. of pale yellow leaflets, m. p. 231—233°. This material is sufficiently pure for most purposes, but repeated crystallisation from aqueous methyl alcohol furnished fine, colourless needles, m. p. 234—235° (Found : C, 62·3; H, 4·4. $C_{15}H_{12}O_6$ requires C, 62·5; H, 4·2%). The alcoholic solution gives an intense reddish-violet coloration on the addition of ferric chloride. On acetylation with boiling acetic anhydride in presence of a little pyridine, the *triacetyl* derivative is obtained and may be crystallised from alcohol in colourless, lustrous needles, m. p. 115—116° (Found : C, 61·0; H, 4·4. $C_{21}H_{18}O_9$ requires C, 60·9; H, 4·3%). It should be noted that inefficient hydrolysis of the ketimine results in nitrogenous products which, although crystalline and consisting largely of benzoyloxyphloracetophenone, cannot be employed in the following syntheses.

Galangin (I).—A stirred mixture of ω-benzoyloxyphloracetophenone (7·4 g.), benzoic anhydride (30 g.) and sodium benzoate (6 g.) was heated (oil-bath at 165—170°) for 3 hours and worked up as in similar cases. Alcohol (80 c.c.) and 10% alcoholic potassium hydroxide (188 c.c.) were employed in the hydrolysis and the light buff crude product (6·4 g.) was boiled for 1 hour with acetic anhydride (20 c.c.) and a drop of pyridine. After decomposition with water,

the triacetyl derivative was collected, and after one crystallisation from alcohol weighed 4·3 g. Repeated crystallisation gave 1·5 g. of colourless, lustrous needles, m. p. 142·5—143·5° (Found: C, 63·5; H, 4·2. Calc. for $C_{21}H_{16}O_8$: C, 63·6; H, 4·0%). Jahns (*Ber.*, 1881, **14**, 2807) and Kostanecki, Lampe and Tambor (*Ber.*, 1904, **37**, 2803) both state that the triacetyl derivative of natural and synthetic galangin has m. p. 142°. The triacetylgalangin (0·6 g.) was hydrolysed by heating with 10% aqueous potassium hydroxide for 1 hour on the steam-bath and the yellow precipitate obtained on acidification of the orange-yellow solution was isolated (0·4 g.). The substance crystallised from aqueous methyl alcohol in yellow needles, m. p. 214—215° (Found, in air-dried material: loss at 100° in a vacuum, 6·2. $C_{15}H_{10}O_5$, H_2O requires H_2O, 6·3%). The fact that galangin forms a hydrate has been previously observed by Jahns (*loc. cit.*). The m. p. of the substance was not depressed by admixture with an authentic specimen of the flavonol.

Kaempferide (II).—A mechanically stirred mixture of ω-benzoyloxyphloracetophenone (7·4 g.), anisic anhydride (40 g.) and sodium anisate (7·5 g.) was heated at 165—170° for 3 hours and then crushed and boiled with alcohol (100 c.c.) for 20 minutes. On the gradual addition of 10% alcoholic potassium hydroxide (200 c.c.) a granular, yellow precipitate was formed and the mixture was boiled for 30 minutes. The alcohol was removed by distillation and carbon dioxide precipitated 4·2 g. from the aqueous solution of the orange-brown residue. Acetylation and crystallisation of the product from alcohol (charcoal) furnished light fawn needles (2·7 g.), m. p. 190—192°, and by recrystallisation, slender, colourless needles, m. p. 193—194° (Found: C, 62·0; H, 4·5. Calc. for $C_{22}H_{18}O_9$: C, 62·0; H, 4·2%). Hydrolysis of the *triacetyl* derivative (1·0 g.) gave a yellow crude product (0·8 g.) which was repeatedly crystallised from methyl alcohol, finally giving long, golden-yellow needles, m. p. 225°. (Loss on heating at 110° for 40 hours, 9·4. Found, in heated material: C, 63·9; H, 4·2. $C_{16}H_{12}O_6,CH_4O$ requires CH_4O, 9·6%. Calc. for $C_{16}H_{12}O_6$: C, 64·0; H, 4·0%). The substance sublimes in extremely fine, silky needles. An alcoholic solution becomes olive-green on the addition of ferric chloride, the tone being browner than that produced by galangin. The *lead* salt is an orange-yellow precipitate, and the *potassium* salt, obtained by means of methyl alcoholic potassium acetate, is a yellow precipitate which is decomposed by boiling water. The lemon-yellow solution of the flavonol in sulphuric acid exhibits a brilliant bluish-green fluorescence which soon becomes greenish-blue.

Benzoylvanillic Acid. (VIII).—This substance, m. p. 178°, was obtained by Tiemann and Kraaz (*Ber.*, 1882, **15**, 2068) by the

oxidation of benzoyleugenol; we have employed the following method: Benzoyl chloride (62·5 g.) was vigorously shaken with a solution of vanillic acid (50 g.) in aqueous sodium hydroxide (48 g. in 800 c.c.) until the odour of the chloride had disappeared. The mixture of acids precipitated by hydrochloric acid was extracted with two successive volumes of boiling water (900 c.c.), the undissolved product being also well washed on the filter and then dried (yield 47·4 g.; 58·4%). This material has m. p. 161—164° and may be employed for most purposes.

Benzoylvanilloyl Chloride, $BzO{\cdot}C_6H_3(OMe){\cdot}COCl$.—An intimate mixture of benzoylvanillic acid (20 g.) and phosphorus pentachloride (19 g.) soon became a semi-fluid mass and the reaction was completed by heating on the steam-bath for 1 hour. The phosphoryl chloride was removed by distillation under diminished pressure and the residue dissolved—a slow process—in boiling light petroleum (350 c.c.; b. p. 60—80°). The filtered solution deposited clusters of slender, white needles (yield 18·7 g.), which, crystallised from light petroleum, had m. p. 96—98° (Found: C, 61·9; H, 4·0; Cl, 12·2. $C_{15}H_{11}O_4Cl$ requires C, 62·0; H, 3·8; Cl, 12·2%). The substance is sparingly soluble in light petroleum, moderately readily soluble in acetone, and very readily in benzene, chloroform, and ether.

Benzoylvanillic Anhydride.—Anhydrous pyridine (100 c.c.) was gradually added with vigorous shaking to a solution and suspension of finely-powdered benzoylvanillic acid (36 g.) and benzoylvanilloyl chloride (40 g.) in dry ether (500 c.c.). On the following day the mixture was shaken for 10 minutes with crushed ice and filtered, the granular solid being then triturated successively with ice-cold water, ice-cold, very dilute hydrochloric acid, and ice-cold aqueous sodium carbonate, and finally washed with water and dried in a vacuum (yield 65 g.), m. p. 169—173°; the material was employed in the synthesis of *iso*rhamnetin without further purification. The substance crystallises from ethyl acetate in slender, cream needles, m. p. 179—180°, after softening at 172° (Found: C, 68·5; H, 4·6. $C_{30}H_{22}O_9$ requires C, 68·4; H, 4·2%). It is sparingly soluble in cold alcohol and acetic acid, moderately readily in benzene and cold ethyl acetate, readily in chloroform, and very sparingly in ether and light petroleum.

iso*Rhamnetin* (III).—Benzoylvanillic anhydride (92·4 g.), sodium benzoylvanillate (11·9 g.) and ω-benzoyloxyphloracetophenone were ground together and the mixture was heated at 180—185° for 6·5 hours; mechanical stirring was used until the hardening of the mass prevented it. After cooling, the flask was broken and the brittle product was powdered, added to alcohol (400 c.c.), and the mixture boiled for 20 minutes. A solution of potassium hydroxide (68·5 g.)

in water (100 c.c.) was then gradually introduced and, after boiling for a further 30 minutes, the alcohol was removed by distillation. The filtered solution of the residue in 600 c.c. of water was diluted to 900 c.c. and saturated with carbon dioxide. After a day, the product was collected (5·43 g.) and 4·4 g. of it were acetylated in the usual manner. The *tetra-acetyl* derivative crystallised from alcohol in long, slender, colourless needles, m. p. 203—205° (yield 2·33 g.), and by further crystallisation the m. p. was raised to 205—207° (Found: C, 59·6; 59·7; H, 4·4, 4·3. Calc. for $C_{24}H_{20}O_{11}$: C, 59·5; H, 4·1%). The derivative is sparingly soluble in methyl or ethyl alcohol, acetic acid, and benzene, moderately readily in acetone or chloroform, and very sparingly in ether. On heating with 10% aqueous potassium hydroxide, hydrolysis and consequent dissolution occur but slowly, and it was found preferable to employ hydrochloric acid for the conversion to *iso*rhamnetin. The tetra-acetate (2·3 g.; m. p. 203—205°) was treated with boiling concentrated hydrochloric acid (200 c.c.) for 1 hour and the bright orange-red precipitate * became pale yellow on the addition of water and was collected (1·52 g.). The substance was crystallised from alcohol and then from acetic acid in greenish-yellow needles, m. p. 305° (decomp.) after darkening at 300°. Power and Salway give the m. p. 295° (decomp.). The crude flavonols obtained by hydrolysis of the glucosides in an aqueous extract of yellow wallflower petals were isolated and purified by solution in aqueous sodium hydroxide and reprecipitation with carbon dioxide. This material was collected and extracted with boiling alcohol, and the extract acetylated in the usual manner. After four crystallisations from alcohol, faintly brown needles, m. p. 185—191°, were obtained. From the vivid fluorescence exhibited in sulphuric acid solution, we judge this product to be contaminated with a kaempferol derivative. It was hydrolysed by means of hot concentrated hydrochloric acid, the flavonol extracted with hot alcohol and the sparingly soluble fraction re-acetylated. After two crystallisations, woolly needles were obtained which, alone or mixed with the synthetic specimen, had m. p. 205—207°. The substance is coloured orange-red by sulphuric acid and dissolves to a yellow solution exhibiting a green fluorescence that becomes bluer and more intense on keeping.

p-*Ethylcarbonato*-m-*methoxybenzoic Acid*,

$$CO(OEt)\cdot O\cdot C_6H_3(OMe)\cdot CO_2H,$$

and its Anhydride.—Vanillic acid was carbethoxylated by a method analogous to that of Fischer (*Ber.*, 1908, **41**, 2877): Ethyl chloroformate (36 g.) was gradually added to an ice-cold, mechanically

* The colour is due to an impurity, since pure synthetical tetra-acetyl *iso*rhamnetin did not exhibit it.

stirred solution of vanillic acid (50 g.) in *N*-aqueous sodium hydroxide (595 c.c.). When the odour of the ester was no longer perceptible, the solution was acidified and the precipitate collected and dried in a vacuum. The product was dissolved in hot acetone, and hot water was added until a turbidity resulted; on cooling, a mass of white needles was deposited and this was collected, washed with aqueous acetone and dried (yield 54·5 g., m. p. 144—146°, and 6·1 g. from the mother-liquor; total 71·4%). The substance separates from a mixture of acetone (2 vols.) and water (1 vol.) in colourless needles, m. p. 147—148° (Found: C, 54·9; H, 5·0. $C_{11}H_{12}O_6$ requires C, 55·0; H, 5·0%). A solution of carbethoxyvanillic acid (60 g.) in thionyl chloride (150 c.c.) was boiled for 45 minutes and the excess of the reagent then removed in a vacuum. The residue was dissolved in dry ether (100 c.c.) and mixed with a suspension of carbethoxyvanillic acid (30 g.) in ether (250 c.c.), and anhydrous pyridine (80 c.c.) was gradually added with shaking. The solid which separated was broken up on the following day, mixed with crushed ice, collected, and well washed with water and with dilute hydrochloric acid (yield 65 g.), m. p. 86—88·5°. p-*Ethylcarbonato*-m-*methoxybenzoic anhydride* crystallises from ethyl acetate in short prisms, m. p. 87—88·5° (Found: C, 57·0; H, 4·6. $C_{22}H_{22}O_{11}$ requires C, 57·1; H, 4·8%).

The authors wish to thank the Department of Scientific and Industrial Research for a grant which has enabled one of them to take part in the investigation and they are also indebted to the Royal Society for grants which have defrayed a part of the cost of the work.

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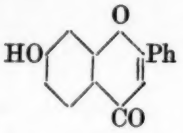
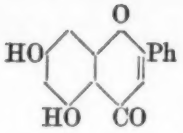
CCCXI.—*A Synthesis of Acacetin and Certain Other Derivatives of Flavone.*

By ROBERT ROBINSON and KRISHNASAMI VENKATARAMAN.

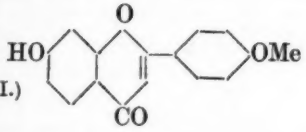
THE direct aroylation of derivatives of *o*-hydroxyacetophenone has hitherto been utilised for the synthesis of 3-substituted flavones only, and in order to extend the scope of this very convenient method we have carefully studied the conditions under which 7-hydroxyflavone (I) and chrysin (II) may best be obtained by benzoylation of resacetophenone and phloracetophenone respectively. Satisfactory yields are obtainable, but relatively more benzoic anhydride and longer

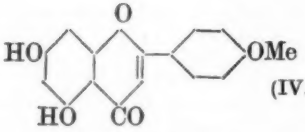
heating are required than with the earlier preparations of flavonol derivatives.

(I.) 

 (II.)

When resacetophenone was treated with anisic anhydride and sodium anisate and the product hydrolysed, 7-hydroxy-4′-methoxyflavone (III) was obtained.

(III.) 

 (IV.)

This substance closely resembles *pratol*, a naturally occurring hydroxymethoxyflavone with which it is very probably identical. Pratol was isolated by Power and Salway (J., 1910, **97**, 231) from *Trifolium pratense*, the common red clover, and Rogerson (*ibid.*, p. 1006) also noted its occurrence among the constituents of *Trifolium incarnatum*, the carnation or crimson-flowered clover. Unfortunately, as the result of a fire all authentic specimens of pratol have been lost, and a direct comparison could not be made. The anisoylation of phloracetophenone and hydrolysis of the product yields acacetin (IV). This flavone was first isolated from the leaves of *Robinia pseudacacia*, Linn., by A. G. Perkin (J., 1900, **77**, 430), who considered that it was probably identical with von Gerichten's apigenin monomethyl ether, prepared by hydrolysis of methylated apiin (*Ber.*, 1900, **33**, 2908). More recently, Hattori (*Acta Phytochim.*, 1925, **2**, No. 3, 105) isolated *acaciin* from the leaves of *Robinia pseudacacia* and showed that the substance is acacetin 7-diglucoside since it could not be methylated by methyl iodide under the usual conditions. The synthetical material was proved, by direct comparison and the method of mixed m. p.'s, to be identical with the natural product derived from acaciin.

Experimental.

7-Hydroxyflavone (I).—A mixture of resacetophenone (5 g.), benzoic anhydride (30 g.) and sodium benzoate (6 g.) was heated at 180—185° for 4 hours, and after cooling, the pale brown mass was broken up and added to alcohol (160 c.c.). The mixture was boiled during the gradual addition of potassium hydroxide (18 g.) dissolved in water (20 c.c.) and then for 30 minutes under reflux. After removal of the greater part of the alcohol by distillation, the residue

was dissolved in water, the filtered solution saturated with carbon dioxide and the precipitated light brown, crude product isolated (5·5 g.). After repeated crystallisation from acetic acid (charcoal) and ethyl acetate, 7-hydroxyflavone was obtained in long, colourless needles, m. p. 240° (Found: C, 75·5; H, 4·3. Calc. for $C_{15}H_{10}O_3$: C, 75·6; H, 4·2%). The yellow solution in sulphuric acid exhibited a blue fluorescence and the acetyl derivative crystallised from alcohol in colourless needles, m. p. 129—130°. The properties of the substance agreed closely with those which Emilewicz and Kostanecki (*Ber.*, 1898, **31**, 703) ascribed to 7-hydroxyflavone.

7-*Hydroxy*-4′-*methoxyflavone* (III).—The starting materials were resacetophenone (4 g.), anisic anhydride * (40 g.), and sodium anisate (4 g.), and hydrolysis was effected by means of potassium hydroxide (20 g.) dissolved in alcohol (200 c.c.). The crude product (3·9 g.) was boiled with an excess of acetic anhydride for 2 hours and on fractional crystallisation of the acetylated material from alcohol three substances (*a*, *b*, *c*,) were isolated. On account of its sparing solubility (*b*) was readily separated from (*a*) and (*c*) and, of these, (*c*) was the more sparingly soluble. The main product (*a*) was repeatedly crystallised from alcohol and 7-acetoxy-4′-methoxyflavone was obtained in small, colourless needles, m. p. 165—166° after sintering at 160° (Found: C, 69·4; H, 4·8. $C_{18}H_{14}O_5$ requires C, 69·7; H, 4·5%). The substance is readily soluble in hot ethyl alcohol, somewhat less readily in hot methyl alcohol, and moderately readily in benzene. On hydrolysis with 10% alcoholic potassium hydroxide, it yields 7-hydroxy-4′-methoxyflavone which crystallises from aqueous alcohol, m. p. 262° (Found: C, 71·2; H, 4·7. $C_{16}H_{12}O_4$ requires C, 71·6; H, 4·5%). On acetylation and crystallisation of the product from a mixture of ethyl acetate and alcohol, clusters of colourless, feathery needles, m. p. 167—168°, were obtained and found to be identical with (*a*). The second product (*b*) is sparingly soluble in hot alcohol and crystallised from ethyl acetate in colourless, slender, rectangular prisms, m. p. 208° (Found: C, 69·8; H, 4·7%). It appears to be isomeric with 7-acetoxy-4′-methoxyflavone, but on hydrolysis it gave rise to two substances. The first and more sparingly soluble of these crystallised from alcohol in bundles of microscopic needles, m. p. 290—291°, dissolving in sulphuric acid to a non-fluorescent, greenish-yellow solution, whilst

* Anisic acid (100 g.) boiled for 24 hours with acetic anhydride (300 g.) furnished 70 g. of the crystallised anhydride, m. p. 99°. Anisic acid (50 g.) was converted into the chloride by thionyl chloride and then allowed to react in benzene solution with anisic acid (45 g.) and pyridine (80 g.). There resulted 75 g. of the crystallised anhydride. The first method is a little more convenient and the second method gives a slightly better yield.

the second substance—long, colourless needles, m. p. 261—262°, from alcohol—was identical with 7-hydroxy-4′-methoxyflavone (Found : C, 71·3; H, 4·8%). The third substance (*c*) from the acetylation of the crude product crystallised in orange-yellow (sometimes almost colourless), large, rhombohedral prisms or decahedra, m. p. 171—172° (Found : C, 69·0; H, 4·5%).

Power and Salway (*loc. cit.*) state that pratol crystallises from alcohol in needles, m. p. 253°, having a talon-like shape with curved edges, and that acetylpratol forms colourless needles, m. p. 166°. Our 7-hydroxy-4′-methoxyflavone crystallised at first in the characteristic form described for pratol, but on recrystallisation very long, straight, colourless needles were obtained. It has frequently been observed that the m. p.'s of flavone and flavonol derivatives synthesised in the present series of investigations were higher than those recorded for the specimens of natural origin. This was the case, *e.g.*, with myricetin and datiscetin (compare *iso*rhamnetin, previous communication) and, from this point of view, the recorded m. p.'s of pratol (253°) and acetylpratol (166°), when compared with those of 7-hydroxy-4′-methoxyflavone (262°) and its acetyl derivative (167—168°), suggest identity. The reactions of the hydroxymethoxyflavone correspond closely with those of pratol. They are : a pale yellow solution in aqueous alkalis ; no coloration with alcoholic ferric chloride ; a yellow coloration on the addition of a drop of sulphuric acid to an acetic anhydride solution ; and, finally, solubility relations. The solution in sulphuric acid exhibits a greenish-blue fluorescence which becomes vivid blue in a short time. Power and Salway have not recorded this behaviour in the case of pratol.

Chrysin (II).—A mechanically-stirred mixture of phloracetophenone * (5 g.), benzoic anhydride (50 g.) and sodium benzoate (6 g.) was heated at 180—185° for 6 hours and, for hydrolysis, alcohol (300 c.c.) and potassium hydroxide (32 g.) in water (20 c.c.) were employed. The crude product was isolated in the usual manner but in this case yellow, crystalline flakes (7·5 g.) were obtained. The material was acetylated by means of an excess of boiling acetic anhydride and a drop of pyridine in 2 hours, and the diacetylchrysin was crystallised from alcohol (charcoal), from benzene–light petroleum, and once again from alcohol in clusters of colourless needles, m. p. 192° (Found : C, 67·5; H, 4·1. Calc. for $C_{19}H_{14}O_6$: C, 67·5; H, 4·1%). Kostanecki (*Ber.*, 1893, **26**, 2901) states that diacetylchrysin has m. p. 185°. On hydrolysis with 10% alcoholic potassium hydroxide (slightly in excess of theoretical) on

* In the preparation of this substance by the method of Hoesch (*Ber.*, 1915, **48**, 1122) it is advantageous to add zinc chloride and to keep the reaction mixture in an ice-chest for a few days.

the steam-bath for 30 minutes and subsequent acidification, chrysin was obtained. The flavone was twice crystallised from methyl alcohol; yellow prisms, m. p. 275° (Found : C, 70·9; H, 3·7. Calc. for $C_{15}H_{10}O_4$: C, 70·9; H, 3·9%). This m. p. is in agreement with that given in the literature and the properties of the substance corresponded closely with those of chrysin as described by Piccard (*Ber.*, 1873, **6**, 884, 1160; 1874, **7**, 888; 1877, **10**, 176), Kostanecki (*loc. cit.*), and Emilewicz, Kostanecki and Tambor (*Ber.*, 1899, **32**, 2448). On methylation in the known manner (Kostanecki, *loc. cit.*), the monomethyl ether, tectochrysin, was obtained. The substance crystallised from alcohol in yellow, hexagonal prisms with pointed ends, m. p. 163° (Found : C, 71·3; H, 4·3. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%). Kostanecki (*loc. cit.*) states that tectochrysin occurs in long needles, m. p. 163°, whilst Piccard (*loc. cit.*) describes hemi-pyramids on a prismatic base and quotes the m. p. 164°.

Acacetin (IV).—The condensation of phloracetophenone (5 g.) with anisic anhydride (50 g.) in presence of sodium anisate (6 g.) and the subsequent hydrolysis were carried out as in the case last described. The crude product (5·8 g.) was crystallised from a mixture of acetic acid and alcohol (charcoal), and recrystallised from 95% alcohol, finally in pale yellow, woolly needles, m. p. 261° (Found : C, 67·5; H, 4·5. Calc. for $C_{16}H_{12}O_5$: C, 67·6; H, 4·2%). A mixture with natural acacetin, m. p. 258—259°, melted at 258—260°, and direct comparison showed that the two specimens were identical in every respect. (We are greatly indebted to Dr. Shizuo Hattori for kindly sending us a specimen of acacetin from acaciin.) The diacetyl derivative of the synthetic flavone was prepared in the usual manner and, as stated by Hattori (*loc. cit.*) for the natural product, it crystallised from alcohol in lustrous needles, m. p. 203° (Found : C, 65·3; H, 4·2. Calc. for $C_{20}H_{16}O_7$: C, 65·2; H, 4·3%).

The authors wish to thank the Royal Society for a grant which defrayed a part of the cost of the investigation.

THE UNIVERSITY, MANCHESTER. [*Received, July 3rd*, 1926.]

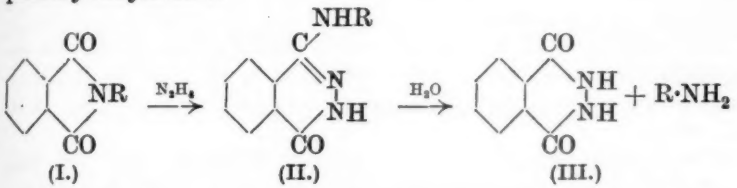
CCCXII.—*A Modification of the Gabriel Synthesis of Amines.*

By HARRY RAYMOND ING and RICHARD HELMUTH FRED MANSKE.

Two modifications of the well-known synthesis of primary amines due to Gabriel have been encountered and constitute distinct improvements where applicable :

(i) It is possible to prepare some alkylphthalimides by heating the alkyl halide with a mixture of phthalimide and potassium carbonate, a method which avoids the troublesome preparation of potassium phthalimide. An excess of the halide is used and is recovered by steam-distillation.

(ii) It is well known that alkylphthalimides are often difficult to hydrolyse. It has now been found that this can easily be achieved indirectly, the condensation product with hydrazine hydrate being readily hydrolysed. Alkylphthalimides (I) react with hydrazine hydrate, in most cases exothermally, to form an intermediate product, probably represented by (II), which is easily decomposed by acids with the formation of phthalylhydrazide (III) and the primary alkylamine.



(I.) (II.) (III.)

This reaction has been applied to the preparation of benzylamine, the three nitrobenzylamines, β-phenylethylamine, ethylenediamine, and trimethylenediamine, the yields in all cases being nearly theoretical. A further application in the synthesis of harmaline will be described in an early communication. Attention may also be directed to a point of some theoretical interest: the attempted preparation of *cyclo*hexylphthalimide, by heating a large excess of *cyclo*hexyl bromide with potassium phthalimide, yielded only *cyclo*hexene and phthalimide. On the other hand, no styrene could be detected as a by-product of the preparation of β-phenylethylphthalimide from β-phenylethyl bromide and potassium phthalimide.

Experimental.

Benzylphthalimide.—An intimate mixture of phthalimide (300 g.) and anhydrous potassium carbonate (150 g.) is treated with benzyl chloride (300 g., 20% excess) and the whole is heated in an oil-bath under reflux for about 3 hours. The excess of benzyl chloride is distilled in a current of steam, and the residual solid benzylphthalimide is filtered and washed with water; yield 360—375 g. One recrystallisation from acetic acid gives the pure product, m. p. 116° (compare Gabriel, *Ber.*, 1887, **20**, 2227).

γ-Bromopropylphthalimide.—In this preparation phthalimide (300 g.), potassium carbonate (150 g.), and trimethylene dibromide (1000 g.) are intimately mixed in a 2-litre Pyrex flask and gradually

heated until reaction begins. It is essential to attach two efficient reflux condensers to prevent loss of alkyl bromide during the subsequent vigorous reaction. At first, the mixture becomes almost solid but as reaction proceeds it becomes mobile again. It is finally heated under reflux for 2 hours in an oil-bath and the excess of trimethylene dibromide distilled in a rapid current of steam (570—590 g. is recovered). The oily residue in the flask solidifies to a pale brown solid which, after filtering, washing, and drying, weighs 480—520 g. It contains as chief impurity $\alpha\gamma$-diphthalimidopropane. After one crystallisation from 400 c.c. of alcohol and drying, the mixture is separated into its constituents by extraction in a continuous apparatus with petroleum ether (b. p. 40—60°), only the bromo-compound dissolving. The yield of pure product, m. p. 72°, is 275—300 g.

The residue, insoluble in petroleum ether, yields, after one recrystallisation from acetic acid, 100—120 g. of pure $\alpha\gamma$-diphthalimidopropane, m. p. 197° (compare Gabriel and Weiner, *Ber.*, 1888, **21**, 2671).

β-*Phenylethylphthalimide.*—Phenylethyl bromide (20 g.) was heated with potassium phthalimide (25 g.) for 2—3 hours at 180—200°. The product was distilled in steam to remove unchanged bromide, the solid filtered, washed with cold alcohol, and recrystallised from acetic acid. β-*Phenylethylphthalimide* is sparingly soluble in cold alcohol and acetic acid, readily in the hot solvents. It melts at 131—132° (Found : N, 5·9. $C_{16}H_{14}O_2N$ requires N, 5·5%).

Benzylamine.—Finely-powdered benzylphthalimide (1 mol.) was warmed in alcoholic suspension with hydrazine hydrate (1 mol.). A white, gelatinous precipitate was rapidly produced which was decomposed by warming with excess of hydrochloric acid. The insoluble phthalylhydrazide was filtered and washed with water. The filtrate was concentrated to remove alcohol and the cooled solution, after filtration from the small amount of precipitated phthalylhydrazide, made alkaline and extracted with ether. The ether solution was dried with solid caustic potash and evaporated and the benzylamine distilled, b. p. 185—187°. Acetylation yielded benzylacetamide, m. p. 60° (Amsel and Hofmann, *Ber.*, 1886, **19**, 1286). The yield of benzylamine was 90—95% of the theoretical.

The following bases (or their salts) were prepared in an exactly similar manner from the corresponding phthalimides : β-Phenylethylamine, b. p. 200—205°, yield 95% ; *o*-nitrobenzylamine hydrochloride, m. p. 248°, yield 90% ; *m*-nitrobenzylamine hydrochloride, m. p. 220°, yield 90%, nitrate, m. p. 181—182° [Holmes and Ingold (J., 1925, **127**, 1812) give the m. p.'s of these salts as 250° and 214° respectively]; *p*-nitrobenzylamine hydrochloride, m. p. 250°,

yield 80%, nitrate, m. p. 218° [Holmes and Ingold (*loc. cit.*) give the m. p.'s of these salts as 224° and 180—181° respectively]; ethylenediamine, diacetyl derivative, m. p. 172°, yield 90%; trimethylenediamine, b. p. 134—136°, yield 96%.

We wish to thank the Ramsay Memorial Fellowship Trust for a Fellowship awarded to one of us (H. R. I.) and the Commissioners of the Exhibition of 1851 for a Scholarship awarded to the other (R. H. F. M.).

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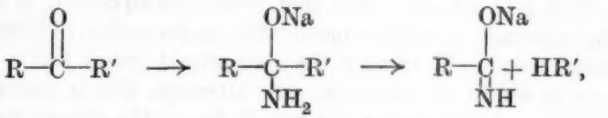
CCCXIII.—*The Fission of Some Methoxylated Benzophenones.*

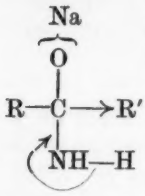
By THOMAS RUSSELL LEA and ROBERT ROBINSON.

THE study of the nitration of catechol and quinol dialkyl ethers gave results which Allan, Oxford, Robinson and Smith (this vol., p. 401) found to be in harmony with a theory of general and alternating polar effects of substituents due to electron displacements of three types. These are (1) a general unidirectional displacement experienced in a particular chain of atoms, (2) a similar general displacement distributed over the molecule, and (3) a displacement which involves co-valency changes and which, in conjunction with the tendency for electronic configurations of the atoms to be retained undisturbed, is responsible for alternating polarity effects in conjugated systems. We have now investigated the direction of fission of the unsymmetrical benzophenones containing phenyl, *m*-methoxyphenyl, anisyl, and veratryl groups, and in considering the subject we propose to employ the above-mentioned electronic theory. When our experiments were nearing completion, Schönberg, Abelsdorff, Kirchrath, Malchow, and Rosenbach (*Annalen*, 1924, **436**, 205) published an account of an investigation of the fission of various substituted benzophenones by means of sodamide, a reaction first observed by Haller and Bauer (*Compt. rend.*, 1908, **147**, 824). The suggested mechanism of the reaction (Schönberg) was

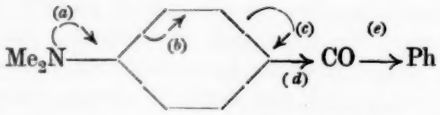


and with this we are in full agreement. The electronic changes

nvolved in the final phase are illustrated in the annexed expression

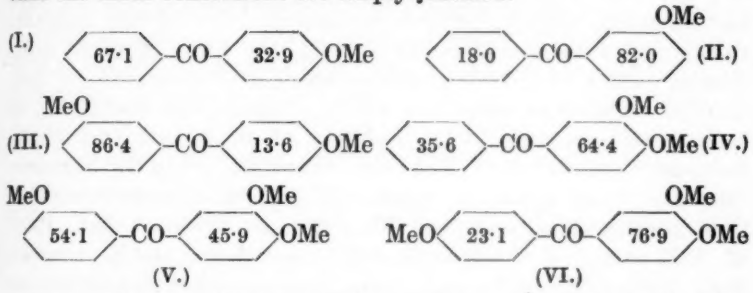


in which the chief points involved are (1) that the free energy of the anion is reduced as the result of the formation of the carboxylamide group (compare Robinson, *Ann. Report*, 1923, **20**, 118, for a similar consideration relating to the benzil–benzilic acid transformation) and (2) that the group R′ retains possession of the electrons covalently held with carbon, and hydrogen is removed from the amino-group as a proton. It follows that R·CO·NH_2 and R′H should be obtained in relatively greater amount than R′·CO·NH_2 and RH if (*a*) R·CO·NH_2 is a stronger acid than R′·CO·NH_2, the comparison being almost certainly parallel with that of the corresponding carboxylic acids, and if (*b*) R′ adheres to electrons more tenaciously than R. The factors work in opposite directions and from the data already accumulated it is clear that (*a*) is of small significance compared with (*b*), a circumstance which is doubtless connected with the irreversible character of the reaction under the conditions obtaining. For example, in phenyl *tert.*-butyl ketone the general effects of the methyl and phenyl groups are represented in the expression Ph←CO←C←Me_3, and it is obvious that this harmonises, so far only as (*b*) is concerned, with the production of benzene and trimethylacetamide from the ketone by the action of sodamide (Haller and Bauer, *Compt. rend.*, 1909, **148**, 70). In the case of *p*-dimethylaminobenzophenone there are electronic displacements due to conjugation (*a*, *b*, *c*) :

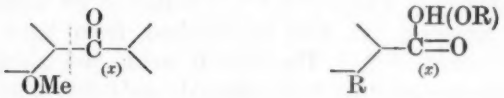


The increased density of electrons associated with the carbon atom in the *p*-position to the dimethylamino-group must tend to repel (*d*) those which are covalently held with the carbonyl carbon. The process (*e*) is thus favoured and therefore the chief products should be, as they are in fact (Schönberg, *loc. cit.*), *p*-dimethylaminobenzamide and benzene. Only one case is known which presents difficulty from the above point of view : Haller and Benoist [*Ann. Chim.*, 1922, (ix), **17**, 25] found that benzoyl*cyclo*propane is decomposed by sodamide in moist benzene with the formation of benzamide and *cyclo*propane. Evidently the *cyclo*propyl group has a strong tendency to retain its electrons, but, although this is unexpected, it should be recognised that our knowledge of the effects produced by the *cyclo*propyl group is not extensive. Haller and Benoist

observed similar results with 1-benzoyl-1-methyl*cyclo*propane but 1-benzoyl-1-benzyl*cyclo*propane gave benzene and 1-benzyl*cyclo*propane-1-carboxylamide. Turning to the methoxybenzophenones, the effect of a *p*-situated group may be considered from the point of view already exemplified in the case of the *p*-dimethylamino-group, whilst, on the other hand, the *m*-methoxyphenyl group has a greater attraction for electrons than phenyl has (compare Oxford and Robinson, this vol., p. 385). The electronic theories accordingly lead us to anticipate that the bond between *p*-methoxyphenyl and carbonyl will be less readily broken than that between phenyl and carbonyl and that the latter bond will be less readily broken than the bond between *m*-methoxyphenyl and carbonyl. The results are given in the following scheme as percentage fissions of the bonds connecting the respective groups to carbonyl and it will be seen that the main conclusions are amply justified.



The results are tolerably consistent with one another, since the groups concerned range themselves in the same order whichever is taken as the standard of comparison. We fully concur with Schönberg and his collaborators in regard to the fundamental soundness of their method of calculation of limiting values dependent on the yields obtained, but we have taken the view that the losses are due to incomplete reaction and to side-reactions of the benzophenones rather than of their fission products. We have carefully avoided loss of the fission products and the use of methods of isolation which could lead to a separation. Finally, we have observed once more the overwhelming effect of an *o*-substituent. 2-Methoxybenzophenone, and 2 : 4- and 2 : 5-dimethoxybenzophenones gave almost pure benzamide on decomposition with sodamide. The bond which is broken is that which attaches the carbonyl to the group bearing the *o*-substituent, and it is the bond (*x*) which is relatively strengthened.



Steric hindrance often appears to operate in this manner, and in the annexed figure the case of the *o*-substituted benzoic acids (esters) is represented for comparison.

EXPERIMENTAL.

It was found best to make no attempt, by the use of a large excess of sodamide or a prolonged period of reaction, to bring about the decomposition of the whole of the benzophenone derivative. The following conditions were employed in all cases. A solution of the ketone (10 g.) in purified toluene (75 c.c.), to which powdered sodamide (4 g.) had been added, was boiled under reflux for 2—3 hours. After the addition of dilute aqueous sodium hydroxide, the mixture was boiled until ammonia was no longer evolved, then steam-distilled, cooled, and filtered. The filtrate was concentrated and the acids precipitated, collected, washed, dried in a vacuum, and analysed, usually by a determination of methoxyl content. In this way 4-methoxybenzophenone (I) gave 4·6 g. of mixed acids (Found: MeO, 14·6, 14·7%, whence anisic acid in mixture = 71·6, 71·9%). A mixture containing 71·8% of anisic acid and 28·2% of benzoic acid contains 67·1% *molecules* of anisic acid and 32·9% *molecules* of benzoic acid. The other figures quoted in the introduction have been similarly calculated. The acid fission products from 2-methoxybenzophenone (Stoermer and Friderici, *Ber.*, 1908, **41**, 332), from 2 : 4-dimethoxybenzophenone (König and Kostanecki, *Ber.*, 1906, **39**, 4028) and from 2 : 5-dimethoxybenzophenone (Kauffmann and Grombach, *Ber.*, 1905, **38**, 796) were in each case proved to be almost pure benzoic acid. Moreover, the fission under the standard conditions proved difficult in these examples and the yields were poor. 4-Cyanobenzophenone (Ahrens, *Ber.*, 1887, **20**, 2957) gave no trace of benzoic or terephthalic acids, but only 4-benzoylbenzoic acid.

3-*Methoxybenzophenone* (II).—Ullmann and Goldberg (*Ber.*, 1902, **35**, 2814) obtained this substance from *m*-methoxybenzoyl chloride and benzene in the presence of aluminium chloride, but this method is unsatisfactory owing to the auto-condensation of the acid chloride to anthracene derivatives. Phenyl-3-methoxyphenylcarbinol was obtained as an oil (yield 90%) from *m*-methoxybenzaldehyde and phenyl magnesium bromide in the usual manner. The carbinol (50 g.) was oxidised at below 50° for 2 hours by means of a solution of hydrated sodium dichromate (100 g.) and sulphuric acid (80 g.) in water (500 c.c.). The product was collected by means of ether, freed from adhering oil, and crystallised from light petroleum (m. p. 38°; yield 25%). The mixed acids (4·5 g.) which were obtained by decomposition with sodamide and subsequent hydrolysis

consisted of benzoic and *m*-methoxybenzoic acids (Found: MeO, 4·4, 4·4%, whence *m*-methoxybenzoic acid = 21·5%).

Fission of 3 : 4-*Dimethoxybenzophenone.*—The ketone, m. p. 103°, was prepared by the method of Bruggemann (*J. pr. Chem.*, 1896, **53**, 253) and, on fission, 4·5 g. of a mixture of benzoic and veratric acids were obtained (Found: MeO, 15·4, 15·4%, whence veratric acid = 45·2%).

3 : 4′-*Dimethoxybenzophenone* (III).—Powdered aluminium chloride (40 g.) was gradually added with cooling to a mixture of *m*-methoxybenzoyl chloride (40 g., b. p. 242—3°/733 mm.), anisole (30 g.) and carbon disulphide (30 c.c.). The reaction was completed by gentle heating on the steam-bath and the product isolated in the usual manner (yield, 20 g.). 3 : 4′-*Dimethoxybenzophenone* crystallised from alcohol in colourless, rhombic prisms, m. p. 55° (Found: C, 74·4; H, 6·1. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%). The acid mixture (4·3 g.) obtained in the sodamide fission consisted of *m*-methoxybenzoic and anisic acids and had f. p. 174·4°. From the data given below it follows that this is the f. p. of a mixture containing 86·4% of anisic acid and 13·6% of *m*-methoxybenzoic acid.

Mixtures of Anisic Acid and m-*Methoxybenzoic Acid.*

% Anisic acid	100·0	96·81	94·5	92·08	88·84	86·44	82·85
F. p.	183·0°	181·0°	179·6°	178·1°	176·1°	174·5°	172·2°

The corresponding graph is a straight line.

3 : 4 : 3′-*Trimethoxybenzophenone* (V).—This substance was prepared by the method described above for 3 : 4′-dimethoxybenzophenone, substituting veratrole for anisole. It was distilled under diminished pressure and then crystallised from methyl alcohol in small, colourless needles, m. p. 83—84° (Found: C, 70·3; H, 6·2. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%). The *oxime* crystallises from alcohol in rhombic prisms, m. p. 128°. The fission experiment gave 2·8 g. of the mixed acids (Found: MeO, 28·4, 28·5%, whence veratric acid = 58·5%) and a considerable amount of the ketone was recovered unchanged.

3 : 4 : 4′-Trimethoxybenzophenone (VI) (Kostanecki and Tambor, *Ber.*, 1906, **39**, 4026) gave 4·0 g. of the mixed acids (Found: MeO, 24·0, 24·0%, whence veratric acid = 26·4%).

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CCCXIV.—*The Hydrolytic Fission of Some Substituted Dibenzoylmethanes.*

By WILLIAM BRADLEY and ROBERT ROBINSON.

IN the present communication, we submit an account of a quantitative study of the hydrolysis of unsymmetrical derivatives of dibenzoylmethane by means of 1% aqueous sodium hydroxide. A diketone, $R{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}R_1$, usually yields a mixture of $R{\cdot}CO_2H$, $R{\cdot}CO{\cdot}CH_3$, $R_1{\cdot}CO_2H$ and $R_1{\cdot}CO{\cdot}CH_3$, and the plan has been adopted of estimating the proportions of the carboxylic acids which are formed. The reactions examined were carried to completion and concordant results were obtained in the analysis and in control experiments. Calculations from the data recorded in the experimental section lead to the results in the following table which shows the number of molecules of $R{\cdot}CO_2H$ and $R_1{\cdot}CO_2H$, respectively, derived from 100 molecules of each of the various diketones, $R{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}R_1$.

R.	R_1.	$R{\cdot}CO_2H$.	$R_1{\cdot}CO_2H$.
o-Methoxyphenyl.	Phenyl.	82·1	17·9
m- „ „	„	61·9	38·1
p- „ „	„	50·2	49·8
*p-iso*Propoxyphenyl.	„	33·0	67·0
m-Chlorophenyl.	„	66·4	33·6
p- „ „	„	63·7	36·3
m-Nitrophenyl.	„	82·3	17·7
p- „ „	„	80·7	19·3
2 : 4-Dimethoxyphenyl.	„	74·7	25·3
3 : 4- „ „ „	„	50·8	49·2
m-Methoxyphenyl.	*p*-Methoxyphenyl.	79·0	21·0
3 : 4 : 5-Trimethoxyphenyl.	Phenyl.	68·8	31·2
m-Methoxyphenyl.	3 : 4-Dimethoxyphenyl.	40·1	59·9
p- „ „	3 : 4- „ „ „	34·2	65·8

α-Anisoylpropiophenone gave 61·1 and 38·9 mols. of anisic and benzoic acids, respectively.

With two exceptions, the stronger * of the acids which might be formed was found to be produced in the greater relative amount, but the existence of any exceptions at all shows that no such simple analysis of the effects of the substituents is possible. Especially striking is the fact that anisic and benzoic acids are obtained in different proportions by the hydrolysis of ω-anisoylacetophenone, $MeO{\cdot}C_6H_4{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}Ph$, and α-anisoylpropiophenone, $MeO{\cdot}C_6H_4{\cdot}CO{\cdot}CHMe{\cdot}CO{\cdot}Ph$.

* As a matter of fact, the dissociation constants of some of the acids concerned have not yet been determined, but in every such case strong analogies are available which enable us to estimate the limits of probable values. For example, the strength of *m*-methoxybenzoic acid has not been directly determined, but it should be slightly stronger than benzoic acid in view of the fact that veratric acid is slightly stronger than anisic acid.

It became apparent that the condition of the tautomeric system in the dibenzoylmethanes has an important bearing on the direction of the hydrolytic fission, and that this should be the case follows also from a consideration of the probable mechanism of the reaction. In this connexion, the following suggestions appear to accord best with modern conceptions. (1) The hydrolytic fission of dibenzoylmethanes is a reaction characteristic of the diketonic phases and does not occur in the keto-enolic modifications. Satisfactory evidence is available in support of this proposition and it will suffice to note that compounds of fixed open-chain β-diketonic structure are readily hydrolysed by alkalis whereas substances having fixed keto-enolic structures and related to β-diketones are relatively stable to hydroxyl ions. (2) On account of the consideration given in (1), the extent of enolisation, great as it is, and the nature of the enols do not affect the result of hydrolytic fission except as mentioned below. (3) The hydrolysis is probably the result of the decomposition of a complex anion formed from the diketone and hydroxyl ion:

$$R{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}R_1 + OH' \longrightarrow R{\cdot}\overset{\overset{O'}{|}}{C}{\cdot}CH_2{\cdot}CO{\cdot}R_1 \longrightarrow R{\cdot}\overset{\overset{O'}{|}}{C}{:}CH{\cdot}CO{\cdot}R_1 + H_2O$$
$$\qquad\qquad\qquad\qquad\quad \underset{OH}{|}$$
$$\qquad\qquad\qquad\qquad\quad \swarrow$$
$$R{\cdot}CO_2' + H{\cdot}CH_2{\cdot}CO{\cdot}R_1$$

The complex ion may undergo other transformations of which the most important is the formation of the enolic modifications as illustrated in the above scheme. (4) Hence the chief factors controlling the direction of the change are (*a*) the rates of formation of the two possible complex anions, $R{\cdot}CO'(OH){\cdot}CH_2{\cdot}CO{\cdot}R_1$ and $R{\cdot}CO{\cdot}CH_2{\cdot}CO'(OH){\cdot}R_1$, and (*b*) the extent to which each of these breaks down with the formation of carboxylate ions. The factor (*a*) should be connected with the relative degree of positive polarity exhibited by the carbonyl groups and therefore with the dissociation constants of the acids $R{\cdot}CO_2H$ and $R_1{\cdot}CO_2H$. As we have already pointed out, a great majority of our experimental results are in accord with this view. A second group of factors influencing (*a*) concerns the nature of the reagent and the solvent, but in the present series these conditions are approximately constant. If, in a certain time, x and x' hydroxyl ions become attached to the groups $R{\cdot}CO{\cdot}$ and $R_1{\cdot}CO{\cdot}$, respectively, and if ax and $a'x'$ represent the numbers of the resulting complex ions respectively which, chiefly by formation of the enols, do not undergo fissions, then we find:

$$R{\cdot}CO_2H \text{ obtained}/R_1{\cdot}CO_2H \text{ obtained} = (1 - a)x/(1 - a')x'.$$

It is beyond our power in the present state of knowledge to develop this expression in any exact manner from a theoretical point of view, but its form shows that the results we have recorded above are not necessarily opposed to the theory. The ratio x/x' may be connected in some relatively simple manner with the dissociation constants of the acids $R{\cdot}CO_2H$ and $R_1{\cdot}CO_2H$, and on the most plausible assumptions of this kind (*e.g.*, that $x/x' = \log K/K'$) we find that the remarkable effect of the substitution of methyl for hydrogen in ω-anisoylacetophenone is susceptible of a simple explanation. The introduction of the methyl group decreases the extent to which each of the complex ions breaks down into a related enol, but this effect is proportionately greater in the case of the formation of the enol, $Ph{\cdot}CO{\cdot}CMe{:}C(OH){\cdot}C_6H_4{\cdot}OMe$ than in that of the enol, $Ph{\cdot}C(OH){:}CMe{\cdot}CO{\cdot}C_6H_4{\cdot}OMe$. In other words, the inhibition of the production of an enol is more efficient in the case of the weaker enol. The assumption that the enol mentioned first above is the weaker is justified by the consideration that the mechanism of the formation of $-C(O)' = CH-$ from $-CO{\cdot}CH_2-$ should be analogous to that of $-CO'_2$ from $-CO{\cdot}OH$ and by the fact that anisic acid is weaker than benzoic acid. We do not here attempt a more detailed discussion of the results, since experiments are in progress which should enable us to evaluate approximately the ratio x/x'.

EXPERIMENTAL.

ω-Anisoylacetophenone.—This substance has been prepared by the action of sodium ethoxide on anisylideneacetophenone dibromide (Pond and Maxwell, *J. Amer. Chem. Soc.*, **1899**, **21**, 966). We obtained it by the condensation of ethyl anisate with acetophenone or of ethyl benzoate with *p*-acetylanisole, the latter process giving the better yield. Powdered sodamide (5 g.) was quickly added to a solution of *p*-acetylanisole (15·4 g.) and ethyl benzoate (15·4 g.) in dry ether (70 c.c.). When the vigorous reaction subsided the mixture was heated on the steam-bath for 4 hours. The bulky sodio-derivative was collected, washed with ether, added to ice-cold dilute acetic acid, and the diketone taken up in ether. On prolonged shaking of the extract with aqueous cupric acetate, a voluminous precipitate of the copper derivative was obtained (26·5 g.). The substance crystallises from benzene in minute, green needles, m. p. 241° (decomp.) (Pond and Maxwell, *loc. cit.*, give 247—249°). On decomposition with dilute sulphuric acid in presence of ether the free anisoylacetophenone was obtained (22·5 g.). The m. p. after crystallisation from alcohol was 132° (Found: MeO, 12·3. Calc. for $C_{16}H_{16}O_3$: MeO, 12·2%).

Phenylanisyldiveratrocopyrine (compare Lawson, Perkin, and

Robinson, J., 1924, **125**, 648) was readily obtained by condensation of the diketone with diaminoveratrone in boiling acetic acid solution. It is very sparingly soluble and crystallises from hot alcohol in almost colourless needles, m. p. 352° (decomp.). The bright yellow *hydrochloride* crystallises in needles and is readily soluble in water. The *acetate* is more stable than that of diphenyldiveratrocopyrine, but is decomposed by water with formation of the free base.

The hydrolysis of ω-anisoylacetophenone (1·75 g.) was effected by gentle warming with 1% aqueous sodium hydroxide (27·55 c.c. = 1 mol.) until the separation of the simple ketones appeared to be complete. Finally the solution was boiled until the odour of acetophenone and acetylanisole was faint. The last traces of neutral material were removed by extraction with ether and the aqueous solution was concentrated to 5—7 c.c. and acidified at 0° by means of 32% hydrochloric acid (1·2 c.c.). The precipitate was collected, washed with ice-cold 10% hydrochloric acid and dried in a desiccator over sulphuric acid and sodium hydroxide to constant weight (Found: MeO, 11·4, 11·5, 11·4%, whence anisic acid in the mixture = 55·9%). All the diketones were hydrolysed in a similar manner and in all cases the reaction was smooth and complete. In no case did the solubility of one of the acids in water reach a value which could materially influence the results (*e.g.*, benzoic acid at 0°, 0·17; anisic acid at 25°, 0·0226%). Particular attention was directed to the technique of the estimations of methoxyl, and control experiments showed that a slightly modified Zeisel-Perkin method is capable of considerable accuracy (Found in anisic acid: MeO, 20·37, 20·39. Calc.: 20·395%).

ω-2-*Methoxybenzoylacetophenone*.—14·6 G. of the copper derivative of this substance resulted from the condensation of ethyl *o*-methoxybenzoate (18 g., b. p. 261—262°) with acetophenone (12 g.) in ethereal solution in presence of sodamide (5 g.). The diketone is readily soluble in most organic solvents and crystallises from ethyl alcohol in rosettes of slender, pale yellow needles, m. p. 65° (Found: C, 75·7; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·5; H, 5·6%). The alcoholic solution becomes deep red on the addition of ferric chloride. The *copper* derivative crystallises from benzene in short, pale green prisms, m. p. 196—197° (decomp.). The diketone reacts slowly with diaminoveratrone and, after 40 hours in boiling glacial acetic acid, a small yield of *phenyl-2-methoxyphenyldiveratrocopyrine* can be isolated. The base crystallises from alcohol in microscopic needles, m. p. 308°. The *hydrochloride* crystallises in clusters of orange-yellow needles, and the yellow solution of the *acetate* in acetic acid is not decolorised on dilution with water nor is any free base precipitated. In this respect, the substance differs markedly from

the isomeric anisylphenyldiveratrocopyrine. The hydrolysis of the diketone by means of the calculated amount of 1% aqueous sodium hydroxide gave a mixture of benzoic acid and *o*-methoxybenzoic acid (Found: MeO, 17·2, 17·6%, whence *o*-methoxybenzoic acid = 85·1%).

ω-3-*Methoxybenzoylacetophenone*.—*m*-Tolyl methyl ether (40 g.) was oxidised on the steam-bath by a solution of potassium permanganate (50 g.) and sodium carbonate (50 g.) in water (2 litres) and when the reaction was completed potassium permanganate (100 g.) dissolved in water (2 litres) was gradually introduced during 5—6 hours. About 8—10 g. of the unchanged ether and 22—25 g. of pure *m*-methoxybenzoic acid were obtained. The acid gave a good yield of the ethyl ester, b. p. 280—283° (or 204°/139 mm.), on treatment with boiling 4% alcoholic hydrogen chloride. Starting from ethyl *m*-methoxybenzoate (13·7 g.), acetophenone (9·1 g.) and sodamide (4 g.), the usual method led to the production of 6 g. of the *copper* derivative of ω-3-methoxybenzoylacetophenone. This crystallised from benzene in small, square, sage-green plates, m. p. 215°. The diketone itself was purified by distillation (b. p. 157—159°/18 mm.) and by crystallisation from alcohol in almost colourless plates, m. p. 59·5° (Found: C, 75·7; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·5; H, 5·6%). The substance is readily soluble in most organic solvents and gives an immediate blood-red coloration with alcoholic ferric chloride. *Phenyl-3-methoxyphenyldiveratrocopyrine* crystallises from *n*-butyl alcohol in faintly yellow needles, m. p. 315°; it is intermediate in basic character between the isomerides mentioned above, which it resembles in most respects. On hydrolysis of the diketone in the usual manner, a mixture of *m*-methoxybenzoic and benzoic acids was obtained (Found: MeO, 13·7, 13·6%, whence *m*-methoxybenzoic acid = 66·9%).

α-*Anisoylpropiophenone*.—Smedley (J., 1910, **97**, 1492) has commented on the difficulty experienced in alkylating dibenzoylmethane by a direct method and we have been unable to find conditions for the methylation of ω-anisoylacetophenone. Unsuccessful experiments were made in alcoholic solution and with the sodium and copper derivatives of the diketone in benzene. This is merely the extreme case of the operation of a tendency already apparent in the case of ethyl benzoylacetate which is far more difficult to alkylate than is ethyl acetoacetate (compare Hope and Perkin, J., 1909, **95**, 2042). The desired substance can be obtained by the condensation of ethyl benzoate and *p*-methoxypropiophenone under the usual conditions, but not a trace could be isolated as the result of a similar experiment with ethyl anisate and propiophenone. *p*-Methoxypropiophenone has been obtained by Gattermann (*Ber.*, 1890, **23**, 1199) and the following modification of the method constitutes a consider-

able improvement: Powdered aluminium chloride (105 g.) was added to a mixture of anisole (75 g.) and carbon disulphide (200 c.c.); thereafter, propionyl chloride (67 g.) was introduced during 20—30 minutes. The product was isolated in the known manner and 70—75 g., b. p. 178—180°/46 mm., were obtained. The condensation of *p*-methoxypropiophenone (16·5 g.) and ethyl benzoate (16 g.) in ethereal solution by means of sodamide (5 g.) proceeded very readily in the cold and gave a copious deposit of the sodio-derivative from which 8 g. of the crude diketone were obtained in the usual way. The ethereal filtrate treated with a further quantity (2·5 g.) of sodamide gave as much again of the crude product. *α-Anisoylpropiophenone* crystallises from alcohol in pale yellow plates, m. p. 56·5° (Found: C, 75·3; H, 5·4. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%). In some other cases persistent low values for carbon and hydrogen were experienced using copper oxide tubes, but at a later stage the difficulty was overcome by the use of lead chromate tubes. This diketone gives a blood-red coloration with ferric chloride in alcoholic solution, its *copper* derivative is readily soluble in benzene and very sparingly soluble in methyl alcohol, from a hot solution in which it crystallises in flat-pointed prisms, m. p. 218°. An interesting confirmation of the constitution of the compound is derived from the fact that it does not yield a copyrine derivative on attempted condensation with diaminoveratrone. The diketone is more readily soluble in, and more readily hydrolysed by, 1% aqueous sodium hydroxide than ω-anisoylacetophenone. The acid mixture from the hydrolysis consisted of benzoic and anisic acids (Found: MeO, 13·5, 13·5%, whence anisic acid = 66·3%).

p-iso*Propoxybenzoic Acid.*—Sodium (4·8 g.) was dissolved in dry *iso*propyl alcohol (70 c.c.) and *p*-bromophenol (40 g.) added to the solution. After the introduction of *iso*propyl iodide (35 g.) the liquid was boiled under reflux until it was neutral (about 7 hours). After the usual processes the *p*-bromophenyl *iso*propyl ether (45·5 g.) was collected at 230—234°. This ether (22·8 g.) reacted readily in ethereal solution with magnesium (2·6 g.), previously activated by means of methyl iodide, and carbon dioxide was passed through the product for 5 hours. The acid was isolated, crystallised from hot water and dried at 100° (Found: C, 66·6; H, 6·8. $C_{10}H_{12}O_3$ requires C, 66·6; H, 6·7%). The substance separates from water in colourless, elongated, hexagonal plates, m. p. 161°. The *ethyl* ester is a colourless oil, b. p. 279—280°, and on condensation with acetophenone in the presence of sodium a small yield of the dibenzoylmethane (copper derivative, m. p. 227—228°, see below) was obtained. It is better to proceed from ethyl benzoate and *p-iso*propoxyacetophenone.

p-iso*Propoxyacetophenone*.—This substance, m. p. 38—39°, b. p. 152—153°/18 mm., has been obtained in small yield from phenyl *iso*propyl ether, b. p. 182—183°, by condensation with acetyl chloride in carbon disulphide solution and in the presence of aluminium chloride. The chief product was *p*-hydroxyacetophenone and it is apparent that dealkylation is far more facile in this case than in that of *p*-methoxyacetophenone, since the analogous preparation of the latter ketone proceeds satisfactorily. The result is in full accord with the requirements of the theory of the general polar effect of alkyl groups. The ketone was prepared by the action of *iso*propyl bromide (6·5 g.) on the sodium salt of *p*-hydroxyacetophenone (from 7 g. of the phenol) in boiling *iso*propyl alcoholic solution (20 c.c.) for 48 hours. 5 G. of a neutral oil, b. p. 153°/26 mm., solidifying to large colourless crystals, m. p. 38—39°, were isolated. The substance crystallises from light petroleum in plates and dissolves in sulphuric acid to a crimson solution (Found: C, 74·0; H, 7·9. $C_{11}H_{14}O_2$ requires C, 74·1; H, 7·8%).

ω-4-iso*Propoxybenzoylacetophenone*.—The condensation of *p-iso*propoxyacetophenone (5 g.) and ethyl benzoate (5 g.) in ether (15 c.c.) was carried out with the help of granulated sodium * (0·65 g.) in 3 days. The isolation was through the copper derivative, the formation of which is very slow in comparison with that of most dibenzoylmethanes. On the other hand, the chlorodibenzoylmethanes form their copper derivatives with great readiness and we connect these phenomena with the relative strengths of the enols as acids. *Copper* iso*propoxybenzoylacetophenone* crystallises from benzene in short, pale green needles, m. p. 228° (Found: Cu, 10·3. $C_{36}H_{34}O_6Cu$ requires Cu, 10·2%). The free diketone crystallises from light petroleum in pale yellow, flat, pointed needles, m. p. 73° (Found: C, 76·6; H, 6·3. $C_{18}H_{18}O_3$ requires C, 76·6; H, 6·4%). This substance is readily soluble in most organic solvents and its alcoholic solution develops an intense crimson coloration on the addition of ferric chloride. *Phenyl*-4-iso*propoxyphenyldiveratrocopyrine* crystallised in pale yellow needles when water was slowly added to a hot solution in acetic acid. The base does not melt below 355° and its *hydrochloride* crystallises in orange needles which are soluble in water. The hydrolysis of *iso*propoxybenzoylacetophenone was carried out under the usual conditions and a mixture of benzoic acid and *p-iso*propoxybenzoic acid was isolated (Found: equivalent, 141·7, 140·7, whence benzoic acid = 57·9%). It may be mentioned here that *p*-ethoxybenzoic acid, obtained from

* In most cases we prefer to employ sodamide, but this reagent varies very much in quality and, encountering unsatisfactory material, we turned for a time to the use of sodium.

p-ethoxyphenyl magnesium bromide, has been esterified and condensed with acetophenone.

ω-p-*Ethoxybenzoylacetophenone* crystallises from light petroleum in pale yellow, elongated, quadrilateral plates, m. p. 68°.

ω-*Piperonoylacetophenone* is readily obtained from ethyl piperonylate and acetophenone and crystallises from alcohol in clusters of short, pale yellow needles, m. p. 85·5° (Found: C, 71·8; H, 4·6. $C_{16}H_{12}O_4$ requires C, 71·7; H, 4·5%). The *copper* derivative crystallises from benzene in small, pale green needles, m. p. 179°. *Phenylpiperonyldiveratrocopyrine* crystallises from alcoholic acetic acid in pale yellow needles, m. p. 328°.

ω-3-*Chlorobenzoylacetophenone*.—*m*-Chlorobenzoic acid was prepared from *m*-aminobenzoic acid by an application of the Sandmeyer reaction. A mixture of ethyl *m*-chlorobenzoate (9·2 g., b. p. 245°), acetophenone (7 g.), ether (25 c.c.) and granulated sodium (1·2 g.) was made at 0° and kept for 3 days. The *copper* derivative (yield, 4 g.), which was isolated in the usual manner, crystallises from benzene in needles, m. p. 254°. The diketone itself separated from alcohol in very pale yellow needles, m. p. 70° (Found: C, 69·5; H, 4·2; Cl, 13·7. $C_{15}H_{11}O_2Cl$ requires C, 69·6; H, 4·3; Cl, 13·7%). The alcoholic solution develops an intense red coloration on the addition of ferric chloride. In sulphuric acid, a bright yellow solution is obtained, whereas the alkyloxydibenzoylmethanes (and acetophenones) give a deep crimson solution. *Phenyl-3-chlorophenyldiveratrocopyrine* crystallises from alcoholic acetic acid in elongated, diamond-shaped plates which do not fuse below 355°. The *hydrochloride* crystallises in yellow needles, easily soluble in cold water. On hydrolysis of the diketone under the standard conditions, a mixture of benzoic and *m*-chlorobenzoic acids was obtained (Found: Cl, 16·2, 16·3%, whence *m*-chlorobenzoic acid = 71·7%).

ω-4-*Chlorobenzoylacetophenone*.—The substance was obtained by Bodforss (*Ber.*, 1918, **51**, 216) by the action of alcoholic potassium hydroxide on *p*-chlorobenzylideneacetophenone dibromide. Ethyl *p*-chlorobenzoate (13 g., b. p. 236—238°) was condensed with acetophenone (8·7 g.) in ethereal solution (20 c.c.) by means of granulated sodium (1·7 g.) at 0°. The *copper* derivative (4 g.) was obtained as usual and this substance crystallises from benzene in pale green needles, m. p. 271°. The β-diketone has m. p. 89° as stated by Bodforss. *Phenyl-4-chlorophenyldiveratrocopyrine* closely resembles the isomeride mentioned above and does not fuse at 370°. The hydrolysis of the diketone gave a mixture of *p*-chlorobenzoic and benzoic acids (Found: Cl, 17·8, 17·8%, whence *p*-chlorobenzoic acid = 78·5%).

ω-3-*Nitrobenzoylacetophenone*.—An attempted condensation of ethyl *m*-nitrobenzoate with acetophenone was unsuccessful, but the substance was obtained by the method of Bodforss (*Ber.*, 1916, **49**, 2803). The *copper* derivative was found to be very sparingly soluble in benzene, but readily soluble in pyridine to a deep green solution from which bluish-green crystals of a solvated compound separate. These lose pyridine at 63—65°. The *copper* derivative is deposited free from solvent from aqueous pyridine and has m. p. 298°. *Phenyl*-3-*nitrophenyldiveratrocopyrine* crystallises from dilute acetic acid in pale yellow needles, m. p. 324°. The *hydrochloride*, long, bright yellow needles, is soluble in dilute hydrochloric acid, but is dissociated in contact with water. On hydrolysis the diketone yields a mixture of benzoic acid and *m*-nitrobenzoic acid (Found: C, 52·8, 52·8%, whence *m*-nitrobenzoic acid = 86·4%).

ω-4-*Nitrobenzoylacetophenone*.—Ethyl *p*-nitrobenzoate and acetophenone afford this diketone in very poor yield under the usual conditions. Wieland (*Ber.*, 1904, **37**, 1148) has, however, obtained the diketone from *p*-nitrobenzylideneacetophenone dibromide and we have utilised this process. The *copper* derivative crystallises from pyridine in vivid emerald-green needles, which lose pyridine at 149° and then melt at 305° (Found: loss at 160°, 11·9. $C_{30}H_{20}O_8N_2Cu,C_5H_5N$ requires C_5H_5N, 12·0%). *Phenyl*-4-*nitrophenyldiveratrocopyrine* darkens but does not melt at 355°. It forms a viscous solution in concentrated hydrochloric acid from which orange needles of the *hydrochloride* are deposited. On washing with water, the salt is decomposed with formation of the free base. Hydrolysis of the diketone under the standard conditions was effected, but it is much more difficult than in any other case examined. Doubtless this is due to the enhanced stability of the anion from the enolic modification, which is the result of the entry of the nitroxyl group. The case recalls that of the somewhat similarly constituted 4 : 4′-dinitrodiphenylcarbamide which is exceedingly resistant to hydrolysis by alkaline solutions. The acid mixture had m. p. 206—226° and obviously consisted mainly of *p*-nitrobenzoic acid (Found: C, 53·0, 53·1%, whence *p*-nitrobenzoic acid = 85·1%).

ω-2 : 4-*Dimethoxybenzoylacetophenone* (compare Perkin and Schiess, J., 1904, **85**, 164; Robinson and Turner, J., 1918, **113**, 876).—The *copper* derivative has m. p. 193° when freed from the molecular proportion of benzene with which it crystallises. Condensation of the diketone with diaminoveratrone occurs readily in boiling acetic acid solution. *Phenyl*-2 : 4-*dimethoxyphenyldiveratrocopyrine* crystallises from alcohol, in which it is sparingly soluble, in slender needles, m. p. 296°. The striking effect of a methoxyl, *o*-situated in the

phenyl groups, on the basicity of the derivative, is again observed. The solution of this substance in glacial acetic acid gives no precipitate on dilution with water. On hydrolysis under the standard conditions, 2 : 4-dimethoxybenzoylacetophenone gave a mixture of 2 : 4-dimethoxybenzoic and benzoic acids (Found : MeO, 27·8%, whence 2 : 4-dimethoxybenzoic acid = 81·5%).

ω-*Veratroylacetophenone.*—Acetoveratrone gave poor results in β-diketone syntheses, but ethyl veratrate is a satisfactory starting-point. The condensation with acetophenone has been already described (Gulland and Robinson, J., 1925, **127**, 1493). *Phenylveratryldiveratrocopyrine* is obtained in excellent yield and crystallises from a mixture of nitrobenzene and alcohol in pale yellow needles, m. p. 289°. The *hydrochloride* crystallises in orange needles readily soluble in water, whilst the yellow solution in glacial acetic acid becomes colourless and deposits the free base on dilution with water. Hydrolysis of the diketone was carried out in the usual manner (Found : MeO, 19·9, 20·1, 20·2%, whence veratric acid = 60·6%).

ω-3-*Methoxybenzoyl*-4-*methoxyacetophenone.*—Employing *p*-acetylanisole (6 g.), ethyl *m*-methoxybenzoate (7 g.), sodamide (2 g.) and ether (20 c.c.), a ready condensation occurred and the *copper* derivative (6·5 g.), which crystallises from benzene in pale green needles, m. p. 218°, was isolated in the usual manner. The diketone separates from light petroleum in aggregates of pale yellow, flat needles, and from alcohol in plates, m. p. 91° (Found : C, 71·9; H, 5·7. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·7%). The substance is readily soluble in most organic solvents and develops a deep red coloration with ferric chloride in alcoholic solution. 3-*Methoxyphenylanisyldiveratrocopyrine* crystallises from alcohol in nearly colourless needles, m. p. 290—293°. The yellow *acetate* is hydrolysed in presence of water. On hydrolysis, the diketone yields a mixture of anisic acid and *m*-methoxybenzoic acid, which was thermally analysed.

Mixtures of Anisic and m-*Methoxybenzoic Acids.*

% Anisic acid	62·92	57·44	49·90	45·77	35·3
F. p.	153·3°	149·3°	141·3°	135·2°	115·2°

Composition of the Hydrolysis Product.

Wt. of product in g.	Wt. of anisic acid added in g.	F. p.	% of anisic acid.	% of anisic acid in hydrolysis product.
1·0109	0·3924	143·5°	51·87	23·90
1·0109	0·4761	145·5	53·63	21·62
1·0109	0·5933	149·7	57·75	20·76

3 : 4 : 5-*Trimethoxybenzoylacetophenone.*—Ethyl 3 : 4 : 5-trimethoxybenzoate (12 g.) and acetophenone (6 g.) were condensed to-

gether in ethereal solution (50 c.c.) by means of powdered sodamide (2·5 g.). A very vigorous reaction ensued and after 1 hour this was completed by gentle heating. The *copper* derivative (7·3 g.) was isolated in the usual manner and found to crystallise from benzene in minute green needles, m. p. 254° (Found: Cu, 9·3. $C_{36}H_{36}O_{10}Cu$ requires Cu, 9·3%); on decomposing this in the usual manner with dilute sulphuric acid in the presence of ether, the β-diketone was obtained and crystallised from ether and from alcohol in canary-yellow plates, m. p. 97° (Found: C, 68·6; H, 5·9. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%). The ferric chloride reaction in alcoholic solution is blood-red. *Phenyl*-3 : 4 : 5-*trimethoxyphenyldiveratrocopyrine* is very sparingly soluble and crystallises on the addition of alcohol to its yellow solution in acetic acid in pale yellow needles, m. p. 323°. The *hydrochloride* crystallises in yellow needles, soluble in water, whilst dilution of an acetic acid solution of the *acetate* causes the precipitation of the free base. On hydrolysis, the diketone furnished a mixture of benzoic and 3 : 4 : 5-trimethoxybenzoic acids (Found: MeO, 34·8, 34·7%, whence trimethoxybenzoic acid = 79·2%).

ω-3-*Methoxybenzoyl*-3 : 4-*dimethoxyacetophenone*.—Ethyl *m*-methoxybenzoate and acetoveratrone react very slowly together in conjunction with sodium or sodamide, but on long standing a good yield of the diketone is obtained. Sodium (1·25 g.) cut in thin clean slices was added to a dry ethereal solution of acetoveratrone (9 g.) and ethyl *m*-methoxybenzoate (9 g.). After 3 weeks, the entire product was gradually added to ice-cold dilute acetic acid and the *copper* derivative (7 g.) isolated as in other cases. This substance crystallises from benzene, in which it is sparingly soluble, in pale green needles, m. p. 223°. The diketone was obtained in the usual manner and crystallised from alcohol in elongated prisms, m. p. 78·5° (Found: C, 68·8; H, 5·7. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%). The crystals of this substance have a curious conical, almond-like shape; they are coloured crimson by sulphuric acid and then dissolve to a yellow solution. Addition of ferric chloride to an alcoholic solution produces a blood-red coloration. *Veratryl*-m-*methoxyphenyldiveratrocopyrine* is readily obtained by the general method and crystallises from *n*-butyl alcohol in almost colourless, slender needles, m. p. 301·5°. The *hydrochloride* crystallises in orange needles. The substance is more strongly basic than diphenyldiveratrocopyrine but less strongly basic than phenyl-2-methoxyphenyldiveratrocopyrine. On hydrolysis of the diketone, a mixture of *m*-methoxybenzoic acid and veratric acid was obtained (Found: MeO, 26·2, 26·5, 26·8%, whence veratric acid = 44·5%).

ω-*Anisoyl*-3 : 4-*dimethoxyacetophenone*.—This diketone has been

obtained from ethyl anisate and acetoveratrone using either sodium or sodamide, but the process is slow. A much more facile reaction occurs between ethyl veratrate and *p*-acetylanisole and this was effected as in previous examples. The *copper* derivative crystallises from benzene in pale green needles, m. p. 238° and the β-diketone crystallises from alcohol in lemon-yellow, pointed, almond-shaped needles, m. p. 97° (Found: C, 69·0; H, 5·8. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%). The behaviour towards solvents, ferric chloride, and sulphuric acid was normal. *Veratrylanisyldiveratrocopyrine*, m. p. 300°, is obtained in only a small yield under the usual conditions; the *acetate* crystallises from acetic acid in slender yellow needles. On hydrolysis, the β-diketone gave a mixture of anisic and veratric acids (Found: MeO, 30·4, 30·0, 29·5%, whence veratric acid = 69·8%).

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CCCXV.—*The Action of Hydrazines on Semicarbazones. Part II.*

By WILLIAM BAIRD and FORSYTH JAMES WILSON.

IN Part I (J., 1924, **125**, 2145) it was shown that ketonic semicarbazones could react with phenylhydrazine in boiling toluene solution in two ways:

$$\left.\begin{matrix}CRR'{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2\\ +NH_2{\cdot}NHPh\end{matrix}\right\} \begin{cases}\nearrow NH_3 + CRR'{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NHPh & (1)\\ \searrow NH_2{\cdot}NH{\cdot}CO{\cdot}NH_2 + CRR'{:}N{\cdot}NHPh & (2)\end{cases}$$

yielding either (1) a δ-anilinosemicarbazone, or (2) a phenylhydrazone and semicarbazide (or its decomposition product, hydrazodicarbonamide). Acetophenone- and benzophenone-semicarbazones reacted almost exclusively according to (1), whilst acetonesemicarbazone reacted almost exclusively according to (2).

In view of these results it was decided to make a general study of the behaviour of semicarbazones, both aldehydic and ketonic, on heating with phenylhydrazine: in all, the semicarbazones of seven aldehydes and fourteen ketones have been investigated. The semicarbazones of acetaldehyde, furfuraldehyde, benzaldehyde, anisaldehyde, cinnamaldehyde, and piperonal reacted exclusively according to scheme (2), whereas *n*-heptaldehydesemicarbazone reacted chiefly according to (2), but also to a slight extent according to (1), the yield of δ-anilinosemicarbazone being 8%.

The behaviour of the ketonic semicarbazone varied in each case; in general both the δ-anilinosemicarbazone and the phenylhydrazone were formed. The approximate percentage yields of the δ-anilinosemicarbazone, indicating the extent to which reaction (1) took place, are quoted in brackets after the name of the ketone concerned: Acetone (5); methyl ethyl ketone (0, only the phenylhydrazone being produced); methyl *n*-propyl ketone (0); diethyl ketone (2); methyl *tert.*-butyl ketone (60); di-*n*-propyl ketone (13); di*iso*propyl ketone (90); *cyclo*hexanone (12); 1-methyl*cyclo*hexan-2-one (10); acetophenone (95); methyl benzyl ketone (13); benzylacetone (8); benzophenone (95); and dibenzyl ketone (90).

Examination of the schemes (1) and (2) will show that the groups R and R′ are likely to have an influence on the course of the reaction. If either or both are sufficiently bulky, then the formation of the phenylhydrazone (2) is likely to be inhibited in favour of the anilinosemicarbazone (1) since, in the production of the latter, the phenylhydrazine residue will take up a position more remote from the groups R and R′. On the whole, the experimental results seem to be in agreement with this supposition. Considering the monophenylated ketones, it will be seen that reaction (1) is most pronounced when the phenyl group is contiguous to the carbonyl group, this effect being less noticeable with methyl benzyl ketone and with benzylacetone where the phenyl group is not directly attached to the carbonyl group. In the case of the non-phenylated ketones, the yield of δ-anilinosemicarbazone is comparatively small except with methyl *tert.*-butyl ketone and di*iso*propyl ketone where there is a concentration of methyl groups on one or both of the α-carbon atoms. With the diphenylated ketones, reaction (1) is pronounced with both benzophenone and dibenzyl ketone, the attachment of a phenyl group to each α-carbon atom evidently strongly inhibiting reaction (2).

Other experiments carried out with different hydrazines support these conclusions. Whilst acetonesemicarbazone and phenylhydrazine gave a yield of only 5% of δ-anilinosemicarbazone, α-methyl-α-phenylhydrazine gave a yield of 52% of *acetone-δ-methylanilinosemicarbazone*, $CMe_2{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NMePh$, and αα-diphenylhydrazine gave 80% of *acetone-δ-diphenylaminosemicarbazone*, $CMe_2{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NPh_2$, replacement of hydrogen in the NH group of the hydrazine by methyl or phenyl evidently favouring reaction (1) at the expense of (2). On the other hand, *p*-tolylhydrazine gave only 9% of *acetone-δ-p-toluidinosemicarbazone*, $CMe_2{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NH{\cdot}C_7H_7$, the methyl group in this case being evidently too remote from the reactive amino-group of the hydrazine to have much effect. The same general results were obtained

when α-methyl-α-phenylhydrazine or *p*-tolylhydrazine reacted with benzylacetonesemicarbazone.

Knöpfer (*Monatsh.*, 1910, **31**, 87) had already investigated the replacement of the semicarbazide residue in semicarbazones by the phenylhydrazine residue, the reaction being carried out with phenylhydrazine in boiling alcoholic or glacial acetic acid solution. No regularities were detected, and the formation of δ-anilinosemicarbazones described by us was not mentioned.

The interaction of acetophenonesemicarbazone and α-carbethoxy-α-phenylhydrazine was investigated in the expectation that the reaction would proceed according to the scheme

$$CMePh{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2 + NH_2{\cdot}N(CO_2Et)Ph = CMePh{:}N{\cdot}\underset{\displaystyle C\text{-}}{N}{\cdot}CO{\cdot}\underset{\displaystyle -NPh}{NH} +$$

$NH_3 + EtOH$. The product, however, was *acetophenone-δ-carbethoxyanilinosemicarbazone*, $CMePh{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}N(CO_2Et)Ph$, and efforts to eliminate ethyl alcohol from this compound were unsuccessful. The constitution of this substance was established by hydrolysis into acetophenone and δ-*carbethoxyanilinosemicarbazide hydrochloride*, $NH_2{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}N(CO_2Et)Ph,HCl$, further hydrolysis giving hydrazine, phenylhydrazine, and alcohol.

The thermal decomposition of acetophenone- and benzophenone-δ-anilinosemicarbazones was also investigated. The former gave acetophenonephenylhydrazone, 1-aminourazole and a small quantity of methyl phenyl ketazine. The probable course of the reaction is that the δ-anilinosemicarbazone (I) yields acetophenonecarbohydrazone * (II) and diphenylcarbohydrazide (III)

$$\text{(I.)}\ 2CMePh{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NHPh = \text{(II.)}\ (CMePh{:}N{\cdot}NH)_2CO + \text{(III.)}\ (PhNH{\cdot}NH)_2CO,$$

(II) and (III) then giving acetophenonephenylhydrazone and 1-aminourazole:

$$(II) + (III) = 2CMePh{:}N{\cdot}NHPh + CO\langle\begin{matrix}NH{\cdot}N(NH_2)\\ \text{——}NH\text{——}\end{matrix}\rangle CO.$$

The methyl phenyl ketazine probably results with 1-aminourazole from the decomposition of the carbohydrazone

$$2\,(II) = CMePh{:}N{\cdot}N{:}CPhMe + CO\langle\begin{matrix}NH{\cdot}N(NH_2)\\ \text{——}NH\text{——}\end{matrix}\rangle CO,$$

(II) being known to decompose in this way on heating.

Benzophenone-δ-anilinosemicarbazone when heated to 180—190° for 7 hours gave benzophenonephenylhydrazone as the only recognisable product. Heating for a shorter time (3 hours) at 160—165° gave a different result: besides some unaltered substance, benzo-

* Unpublished work.

phenonecarbohydrazone * was isolated; resinification occurred and diphenylcarbohydrazide could not be isolated, although various colour reactions indicated its presence. Thus the reaction apparently followed the same course as in the previous case except that no ketazine was formed. To test the supposition that the formation of the phenylhydrazone at the higher temperature was due to interaction of the carbohydrazone with diphenylcarbohydrazide, these two substances were heated together and found to yield benzophenonephenylhydrazone and, apparently, 1-aminourazole.

Work on these δ-anilinosemicarbazones will be continued.

Experimental.

Interaction of Semicarbazones and Phenylhydrazine.

Molecular quantities of the two reactants were heated under reflux in toluene solution or suspension at 130—135° until the evolution of ammonia had practically ceased, the time required being indicated in each case. Hydrazodicarbonamide, if formed, was filtered off and identified, and the toluene, unless otherwise stated, was then removed by distillation under reduced pressure and the residue worked up as described. The δ-anilinosemicarbazone, if formed, was characterised by analysis and by hydrolysis with hot dilute hydrochloric acid into aldehyde or ketone and δ-anilinosemicarbazide hydrochloride, previously described.

Acetaldehydesemicarbazone (6 hrs.) and *furfuraldehydesemicarbazone* (10 hrs.). Hydrazodicarbonamide and the aldehydic phenylhydrazone were the only products in each case.

n-*Heptaldehydesemicarbazone* (8 hrs.). Hydrazodicarbonamide was formed; the oily residue on cooling deposited n-*heptaldehyde*-δ-*anilinosemicarbazone* which, after washing with light petroleum and several recrystallisations from absolute alcohol, formed small acicular aggregates, m. p. 176° (yield 8%) (Found: N, 21·5, 21·6. $C_{14}H_{22}ON_4$ requires N, 21·4%). *n*-Heptaldehydephenylhydrazone was identified in the residue from the δ-anilinosemicarbazone by its b. p. and by hydrolysis with dilute sulphuric acid.

Benzaldehydesemicarbazone (10 hrs., 120°). About half of the substance was recovered unchanged, the products being hydrazodicarbonamide and the phenylhydrazone. In xylene solution (6 hrs. at 140—150°) the same reaction was nearly complete.

Anisaldehydesemicarbazone. This reaction, carried out as in the preceding case, gave hydrazodicarbonamide and anisaldehydephenylhydrazone; at the higher temperature, small quantities of the azine were formed.

* Unpublished work.

Cinnamaldehyde- and piperonal-semicarbazones. These reactions, carried out as in the last two cases, gave hydrazodicarbonamide and the phenylhydrazone.

Methyl ethyl ketone semicarbazone (4 hrs., 80—90°). Hydrazodicarbonamide and semicarbazide were formed; the residual oil was identified as the phenylhydrazone by its b. p. and by hydrolysis with acid. Further experiments at higher temperatures and for longer times led to the same results, no δ-anilinosemicarbazone being detected.

Methyl propyl ketone semicarbazone (9 hrs.). Hydrazodicarbonamide was formed; the residual oil was fractioned under reduced pressure and identified as the phenylhydrazone, no δ-anilinosemicarbazone being formed.

Diethyl ketone semicarbazone (7½ hrs.). Hydrazodicarbonamide was formed; addition of 2 vols. of light petroleum to the oily residue gave, on cooling in ice, a *solid* which crystallised from alcohol in plates, m. p. 180—181°, too small in amount to identify. Further addition of light petroleum and cooling in ice deposited a solid which crystallised from alcohol, in which it was fairly soluble, in needles, m. p. 141°. This was *diethyl ketone δ-anilinosemicarbazone* (yield 2%) (Found: N, 24·2. $C_{12}H_{18}ON_4$ requires N, 23·9%). The light-petroleum solution was then evaporated, and the residue on distillation gave a fraction, b. p. 130°/6 mm., identified as diethyl ketone phenylhydrazone by hydrolysis with acid.

Methyl tert.*-butyl ketone semicarbazone* (7½ hrs.). Hydrazodicarbonamide was formed; the toluene filtrate on concentration under reduced pressure deposited crystals of the *δ-anilinosemicarbazone*, further quantities separating on addition of light petroleum and cooling in ice. This substance crystallised from absolute alcohol in silky needles, m. p. 179° (Found: N, 22·5, 22·7. $C_{13}H_{20}ON_4$ requires N, 22·6%); yield 63%. The petroleum–toluene solution was evaporated, and the ketonic phenylhydrazone remained.

cyclo*Hexanonesemicarbazone* (4 hrs.). Hydrazodicarbonamide was formed. The almost solid residue was washed with alcohol and recrystallised from methyl alcohol in plates, m. p. 192°; it was very soluble in hot pyridine and slightly soluble in boiling methyl and ethyl alcohols. It was the *δ-anilinosemicarbazone*, yield 12% (Found: N, 23·0, 22·9. $C_{13}H_{18}ON_4$ requires N, 22·8%). Concentration and freezing of the alcoholic washings deposited *cyclo*hexanonephenylhydrazone, identified by its m. p. and by conversion into tetrahydrocarbazole with sulphuric acid.

1-*Methyl*cyclo*hexan-2-onesemicarbazone* * (8 hrs.). Hydrazodi-

* The ketone was prepared by the method used by Knoevenagel and Tübben for the 1 : 3-compound (*Annalen*, 1897, **297**, 154).

carbonamide was filtered off, in the heat, and the toluene filtrate on cooling in ice deposited the δ-*anilinosemicarbazone* which crystallised from alcohol in needles, m. p. 182—183° (Found: N, 21·6. $C_{14}H_{20}ON_4$ requires N, 21·5%). The toluene solution was then completely evaporated, and the oily residue solidified when cooled in ice. Extraction with hot light petroleum yielded a further quantity of the insoluble δ-anilinosemicarbazone (total yield 10%); the filtrate on evaporation in a vacuum gave a solid residue of the phenylhydrazone, which recrystallised from aqueous alcohol as nearly colourless needles, m. p. 45—46°. As the phenylhydrazone is described as an oil (Plancher, *Atti R. Accad. Lincei*, 1900, **9**, 221), it was prepared by heating the ketone for 1 hour on the water-bath with a slight excess of phenylhydrazine; the ethereal solution of the product was washed with dilute acetic acid and with water, dried and evaporated to dryness in an evacuated desiccator. The residue after crystallisation as above proved to be identical with the phenylhydrazone described by us (Found: N, 13·7. $C_{13}H_{18}N_2$ requires N, 13·9%). It quickly decomposed on exposure, giving a dark oil.

Dipropyl ketone semicarbazone (5½ hrs.). After filtration from hydrazodicarbonamide in the heat and removal of most of the toluene the ketonic δ-*anilinosemicarbazone* was deposited on cooling, the separation being assisted by addition of light petroleum; yield 13%. It crystallised from alcohol in long, silky needles, m.p. 152° (Found: N, 21·5, 21·4. $C_{14}H_{22}ON_4$ requires N, 21·4%); insoluble in light petroleum, sparingly soluble in cold alcohol, fairly soluble in other common solvents. The phenylhydrazone was obtained from the reaction mother-liquors by fractionation under reduced pressure and identified by hydrolysis with acid.

Diisopropyl ketone semicarbazone * (5½ hrs.). No hydrazodicarbonamide was formed; the toluene solution on cooling deposited the δ-*anilinosemicarbazone* which crystallised from alcohol in prismatic needles, m. p. 181° (yield 90%) (Found: N, 21·5, 21·5. $C_{14}H_{22}ON_4$ requires N, 21·4%). No other product was found.

Methyl benzyl ketone semicarbazone (7 hrs.). Hydrazodicarbonamide was formed; addition of light petroleum to the oily residue gave on cooling in ice a solid which was extracted twice with boiling light petroleum. The insoluble residue after several recrystallisations from alcohol gave colourless plates of the δ-*anilinosemicarbazone*, m.p. 181—182° (yield 13%) (Found: N, 19·9, 19·9. $C_{16}H_{18}ON_4$ requires N, 19·9%). Concentration of the petroleum mother-liquors gave crystals of the phenylhydrazone, identified by its m. p. and by hydrolysis.

* The ketone was prepared by the manganous-oxide method from *iso*butyric acid (Sabatier and Mailhe, *Compt. rend.*, 1914, **158**, 832).

Benzylacetonesemicarbazone (8 hrs.). Hydrazodicarbonamide was filtered off and most of the toluene was evaporated. On cooling, the *δ-anilinosemicarbazone* was deposited and more was obtained on addition of light petroleum and allowing to stand (yield 8%). The substance was dimorphous: it crystallised from alcohol in silky needles, m. p. 162°, but from the mother-liquors it separated in plates of the same m. p.; it was slightly soluble in cold alcohol, and easily in ether and benzene (Found: N, 19·0, 19·1. $C_{17}H_{20}ON_4$ requires N, 18·9%). The phenylhydrazone could not be obtained in the solid form from the reaction mother-liquors but was identified by hydrolysis with acid.

Dibenzyl ketone semicarbazone (4 hrs.). The solution gave a nearly solid mass of the *δ-anilinosemicarbazone*, the only product of the reaction (yield 90%). It crystallised from pyridine or glacial acetic acid in very fine needles, m. p. 205°, insoluble or nearly so in the common solvents (Found: N, 15·8, 15·8. $C_{22}H_{22}ON_4$ requires N, 15·6%).

Interaction of Semicarbazones with α-Methyl-α-phenylhydrazine, p-Tolylhydrazine, αα-Diphenylhydrazine, and α-Carbethoxy-α-phenylhydrazine.

With α-Methyl-α-phenylhydrazine.—Acetophenonesemicarbazone (8 hrs.). A clear solution resulted; on cooling, crystals of *acetophenone-δ-methylanilinosemicarbazone* were deposited; after concentration and addition of alcohol further quantities separated on standing (yield 85%). It was recrystallised from alcohol and was moderately soluble in cold pyridine, chloroform, and glacial acetic acid, and sparingly in cold alcohol, ether, acetone, and benzene; prisms, m. p. 196° (Found: N, 19·9, 20·0. $C_{16}H_{18}ON_4$ requires N, 19·9%). This substance, the only product of the reaction, was hydrolysed by boiling with 6% hydrochloric acid, the acetophenone was removed by ether extraction, and the aqueous solution, on evaporation under reduced pressure, gave a residue of *δ-methylanilinosemicarbazide hydrochloride*. It was purified by washing with ether, dissolving in absolute alcohol, in which it was freely soluble, and adding ether or light petroleum: it separated as an oil which solidified on being scratched, m. p. 181° (decomp.) (Found: N, 25·8; Cl, 16·3. $C_8H_{13}ON_4Cl$ requires N, 25·9; Cl, 16·4%).

Acetonesemicarbazone (8 hrs.). The hot solution was filtered from hydrazodicarbonamide; on cooling, crystals of the *δ-methylanilinosemicarbazone* were deposited, more being obtained on concentrating and adding light petroleum (yield 52%). It was sparingly soluble in cold alcohol, from which it crystallised in elongated masses of diamond-shaped plates, m. p. 194° (Found: N, 25·6, 25·5. $C_{11}H_{16}ON_4$

requires N, 25·5%). The petroleum solution contained acetone-methylphenylhydrazone, identified by its b. p. and by hydrolysis.

Benzylacetonesemicarbazone (7 hrs.). A quantity of insoluble material, too small for identification, was formed; the filtrate on evaporation left a viscous oil which solidified on dissolving in ether and evaporating in a vacuum: freezing did not effect solidification. Crystallisation from alcohol gave a sparingly soluble compound, m. p. 213°, too small in amount to identify, and the ketonic *δ-methylanilinosemicarbazone*, acicular rosettes, m. p. 113° (yield 65%) (Found: N, 18·1, 18·1. $C_{18}H_{22}ON_4$ requires N, 18·1%).

n-*Heptaldehydesemicarbazone* (7 hrs.). The toluene solution after filtration from hydrazodicarbonamide was evaporated; addition of light petroleum gave a solid too small in amount to identify. The filtrate from this was evaporated, and the ethereal solution of the residue was washed with dilute acetic acid and water, dried over potassium carbonate and evaporated; on fractionation an almost colourless oil was obtained, b. p. 169—172°/5 mm., and identified by hydrolysis as n-*heptaldehydemethylphenylhydrazone* (Found: N, 12·8. $C_{14}H_{22}N_2$ requires N, 12·8%).

With p-*Tolylhydrazine.—Acetonesemicarbazone* (9 hrs.). After filtration from hydrazodicarbonamide, the solution, on being cooled and scratched, deposited crystals which, after several recrystallisations from alcohol, had m. p. 175—176° (yield 9%). Although the analysis was not very satisfactory (Found: N, 25·0, 24·9. $C_{11}H_{16}ON_4$ requires N, 25·5%), the compound was apparently *acetone-δ-p-toluidinosemicarbazone*. Acetone-*p*-tolylhydrazone was identified in the toluene mother-liquors by its m. p. and by hydrolysis.

Benzylacetonesemicarbazone (8 hrs.). Hydrazodicarbonamide (yield 80%) was filtered off, the residue on crystallisation from light petroleum gave pale yellow needles, m. p. 74—78°, of *benzylacetone-p-tolylhydrazone* (Found: N, 11·3. $C_{17}H_{20}N_2$ requires N, 11·1%). This compound was fairly soluble in light petroleum and decomposed readily. No *δ-p*-toluidinosemicarbazone was formed.

With αα-Diphenylhydrazine.—Acetonesemicarbazone (7 hrs.). No hydrazodicarbonamide was formed; the toluene solution on cooling deposited crystals of the *δ-diphenylaminosemicarbazone*, and further quantities were obtained by evaporation and addition of a little alcohol to the residue; needles, m. p. 186—187°, from alcohol (yield 80%). The substance is dimorphous, the needles on standing in alcohol gradually changing to prisms of the same m. p., this change being accelerated by boiling; the prisms gave needles again on recrystallisation (Found: N, 20·0, 19·9. $C_{16}H_{18}ON_4$ requires N, 19·9%). It gave a pale bluish-green colour with concentrated sulphuric acid, and a very deep bluish-green colour if the sulphuric

acid contained a trace of nitric acid. Aqueous-alcoholic copper sulphate solution gave a pale light-blue colour which gradually changed to a permanganate colour on standing; the colour was unaffected by boiling. Alcohol and ferric chloride gave a similar permanganate colour more rapidly; on boiling this changed to a brownish-red.

Acetophenonesemicarbazone ($8\frac{1}{2}$ hrs.). No hydrazodicarbonamide was produced, the only product being *acetophenone-δ-diphenylaminosemicarbazone* which, after extraction with boiling alcohol to remove a little unaltered semicarbazone, was recrystallised from a mixture of alcohol and pyridine; thick hexagonal plates, m. p. 236—237° (decomp.) (yield 90%); sparingly soluble in the common solvents, easily soluble in pyridine and acetic acid, and giving a bluish-green colour with concentrated sulphuric acid (Found: N, 16·3, 16·4. $C_{21}H_{20}ON_4$ requires N, 16·3%). The substance was hydrolysed by boiling for 2 hours with 12% hydrochloric acid and the aqueous portion, after removal of the acetophenone by ether, was evaporated to dryness under reduced pressure. Extraction with hot absolute alcohol left a residue of hydrazine hydrochloride; addition of dry ether to the filtrate precipitated *δ-diphenylaminosemicarbazide hydrochloride* which was converted into the *benzylidene* derivative in the usual way: long, silky needles from alcohol, m. p. 235—236° (decomp.), giving a bluish-green colour with concentrated sulphuric acid (Found: N, 17·0. $C_{20}H_{18}ON_4$ requires N, 17·0%).

Acetophenonesemicarbazone and α-Carbethoxy-α-phenylhydrazine (10 hrs.).—On cooling, *acetophenone-δ-carbethoxyanilinosemicarbazone* was collected and recrystallised from alcohol as rosettes of acicular plates, m. p. 192°. The substance was dimorphous: on standing in alcohol these crystals changed into thick plates of the same m. p., acicular plates being deposited again on recrystallisation (Found: N, 16·5, 16·5; C, 63·4; H, 5·9. $C_{18}H_{20}O_3N_4$ requires N, 16·5; C, 63·5; H, 5·9%). Decomposition took place on heating above the m. p., only methyl phenyl ketazine being isolated. The substance was hydrolysed by boiling for 5 minutes with dilute hydrochloric acid, and the aqueous portion, after removal of the acetophenone with ether, was evaporated to dryness under reduced pressure. The residual *δ-carbethoxyanilinosemicarbazide hydrochloride* was obtained as a microcrystalline mass by precipitating the absolute-alcoholic solution with ether, m. p. 190° (Found: Cl, 12·9, 12·9. $C_{10}H_{15}O_3N_4Cl$ requires Cl, 12·9%). The *benzylidene* derivative crystallised from alcohol as needles, m. p. 158° (decomp.) (Found: N, 17·0, 17·1. $C_{17}H_{18}O_3N_4$ requires N, 17·2%). The hydrochloride was hydrolysed with difficulty by slow distillation with 50% sulphuric acid, alcohol being detected in the distillate and hydrazine and phenylhydrazine in the residue.

Action of Heat on δ-Anilinosemicarbazones.

Benzophenone-δ-anilinosemicarbazone.—This gave, after 7 hours' heating at 180—190° and cooling, a clear, hard resin which was extracted with ether. The extract was evaporated to dryness in a vacuum and the residue, after being recrystallised from alcohol (charcoal), was found to be benzophenonephenylhydrazone. No other substance was isolated except a small quantity of a *compound*, m. p. 213°. The experiment was repeated (3 hrs. at 160—165°) and the melt when cold was broken up with ether. The crystals which gradually formed were collected, washed with ether and extracted with boiling alcohol, leaving a minute residue. The extract on cooling deposited a solid which was fractionally crystallised from alcohol. Benzophenonecarbohydrazone, m. p. 223—225°, was first obtained and identified by comparison with an authentic specimen (Found : N, 13·2. Calc. : N, 13·4%); unaltered δ-anilinosemicarbazone was also obtained. Many of the crops turned pink on standing, the mother-liquors gave colour reactions which are also given by diphenylcarbohydrazide, but this substance could not be isolated, only resinous products being obtained.

Acetophenone-δ-anilinosemicarbazone.—The substance was heated at 220—225° for 2 hours, a little ammonia being evolved after that time. The cold melt was extracted twice with ether to remove acetophenonephenylhydrazone. The residue was extracted with a little hot alcohol which dissolved methyl phenyl ketazine; the insoluble solid after recrystallisation from water melted at 273—274° (decomp.), and was identified as 1-aminourazole (Found : N, 48·3. Calc. : N, 48·3%).

Action of Diphenylcarbohydrazide on Benzophenonecarbohydrazone.—Molecular quantities of the two reactants were heated to 185° for 8 hours. The cold mass was extracted with ether and ultimately solidified after being scratched. The solid was extracted with boiling absolute alcohol; the residue was very small, but dissolved in water with an acid reaction and appeared to be 1-aminourazole; the alcoholic extract contained benzophenonephenylhydrazone.

In conclusion, we wish to thank the Carnegie Trust for the Universities of Scotland for a research grant which has partly defrayed the expenses of this work. We wish also to thank the Governors of this College for a research assistantship which has enabled one of us (W. B.) to share in this investigation, during part of which he was also holder of the "Nobel Industries Prize," for which thanks are now expressed to Nobel Industries, Ltd.

THE ROYAL TECHNICAL COLLEGE,
GLASGOW.

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CCCXVI.—*The Non-acidic Oxidation Products of Paraffin Wax.*

By FRANCIS FRANCIS and HARRY FREDERICK GAUNTLETT.

THE majority of those who have investigated the products resulting from the oxidation of paraffin by air or oxygen have been concerned with the acidic materials which are formed, and, as regards the non-acidic substances, have stated their amount, speculated as to their nature, and shown that they decreased as the temperature of the oxidation was increased, or as the period of that process was prolonged.

Grun, however, in 1920 (*Ber.*, **53**, 987) attempted to elucidate their nature, and although he did not succeed in isolating in a pure state any of the classes of substances present, nor publish any analyses of his products, yet he showed the presence of alcohols and carbonyl derivatives. The carbonyl compounds were identified as a class, and the approximate amount present was estimated, by the determination of the acetyl value of a mixture containing alcohols before and after reduction. Grun claimed to have obtained stearic acid by the oxidation of a fraction of these carbonyl derivatives, but did not publish any of the constants or analytical values obtained for his product. Even if this acid was isolated, no light is thrown on the nature of its source, since it could have been produced equally well by the simple oxidation of an aldehyde, or by the disruptive oxidation of a ketone.

We have again investigated these non-acidic materials and have succeeded in extending Grun's observations and shown that they consist of secondary alcohols and ketones and their further oxidation products. The work, however, has proved difficult, since we have been unable to find any derivatives of these substances which were capable of purification by crystallisation.

It is certain that this mixture contains the primary oxidation products of paraffin, and since Piper (J., 1925, **127**, 2194) has shown that the hydrocarbons isolated by one of us from paraffin wax are *n*-hydrocarbons, it becomes of importance to determine the nature of the alcohols and carbonyl derivatives present, in order to obtain some knowledge of the points at which air or oxygen first attacks the long carbon chains.

1. *Separation of the Oxidation Products.*—The paraffin used in the investigations which are being carried out in these laboratories is of Scotch origin and melts at 55—56°. As previously described (J., 1922, **121**, 496), it was oxidised at 100° in the presence of 5% of turpentine by a rapid current of dry air over a period of 1200

hours. The resulting material was crystallised from fifteen times its weight of acetone. The oxidation products were relatively soluble, and the main bulk of unchanged paraffin crystallised on cooling. If this process was repeated with these hydrocarbons, they were obtained free from oxidised material, although the soluble oxidised product always contained small amounts of unchanged hydrocarbons. In different experiments the unoxidised hydrocarbons amounted to between 25 and 30% of the crude product from the oxidation; they are capable of further oxidation by the above method.

Approximately one-fifth of the oxidised material recovered from the acetone was composed of anhydrides, and esters constituted a larger proportion of the mixture than the free alcohols. This mixture was saponified in alcoholic solution with excess of caustic potash in order to decompose these substances, and the resulting solution was diluted with water until the whole contained 50%. On repeatedly shaking this solution with large volumes of light petroleum, more than 90% of the non-acidic products were extracted. In different experiments these substances varied between 28 and 39%, and the acidic products, obtained from the solution of their alkaline salts, from 69 to 58%.

2. *Partial Separation of Mono- and Di-oxy-compounds.*—The mixture of alcohols and carbonyl compounds, together with dioxy-derivatives and some unoxidised hydrocarbons—constituting, after saponification, the non-acidic products of the oxidation—may be partly separated into mono- and di-oxy-substances by repeated crystallisation from eight times its weight of acetone.

In different experiments, the white, crystalline mixture of mono-oxy-compounds and hydrocarbons, with small quantities of dioxy-derivatives of the higher hydrocarbons, varied from 62 to 66% of the total non-acidic material.

The dioxy-, with small quantities of polyoxy-, and mono-oxy-derivatives of low molecular weight, constituted between 38 and 34% of the mixture. It formed a brown, non-crystalline, soft wax, very soluble in all organic solvents, and decomposed on distillation in a vacuum.

3. *Treatment of the Mixture of Mono-oxy-substances.*—On fractionating the mono-oxy-mixture in a vacuum of 0·3 mm. it was not found possible to effect a separation of alcohols, ketones and hydrocarbons, although by far the greater part of the dioxy-substances of higher boiling point, which could not be distilled without decomposition, was found in the residue.

The various fractions were then acetylated with acetic anhydride; the products were liquids which deposited a certain quantity of

ketones and hydrocarbons on cooling. The greater part of these impurities crystallised when an acetone solution of the mixture was kept in the ice chamber for some days. The separation of ketones and hydrocarbons is described in section 5.

After the above treatment the lowest-boiling fraction was saponified, and the resulting alcohol converted into the phthalic acid ester. This substance was purified by means of its barium salt, of which two different preparations gave, by titration, *M* (for the alcohol) 337, 328 (Found for the acetate: C, 77·6; H, 13·1. The alcohol $C_{22}H_{46}O$ requires *M*, 326. Its acetate, $C_{24}H_{48}O_2$, requires C, 78·2; H, 13·1%). This indicated clearly the presence of an alcohol of the same carbon content as the lowest hydrocarbon, $C_{22}H_{46}$, known to be present in the paraffin wax used in this work.

The purified acetates obtained from the remaining fractions were again fractionated in a vacuum of 0·1 mm. They boiled between 184° and 220°. In order to determine the alcohols of minimum carbon content the lowest fraction was analysed, and since the highest was contaminated with dioxy-material, an intermediate one was investigated. The results obtained were as follows:

(1) Acetate fraction, b. p. 184—189°. Found: C, 78·6; H, 13·3; sap. value, 140. $C_{26}H_{52}O_2$ requires C, 78·8; H, 13·1%; sap. value, 141. The alcohol obtained from this acetate, on recrystallisation from acetone, melted at 51·5° (Found: C, 80·6; H, 14·4; *M*, ebullioscopic in chloroform, 343. $C_{24}H_{50}O$ requires C, 81·3; H, 14·1%; *M*, 354).

(2) Acetate fraction, b. p. 204—212°. Found: C, 78·2; H, 13·1; sap. value, 135. Mol. refractivity, 128·3. $C_{27}H_{54}O_2$ requires C, 78·9; H, 13·2%; sap. value, 136·8; mol. refractivity, 128·4. The alcohol obtained from this acetate fused at 61·6° (Found: C, 81·4; H, 14·1; *M*, in chloroform, 369. $C_{25}H_{52}O$ requires C, 81·4; H, 14·2%; *M*, 368).

Our thanks are due to Mr. N. E. Wood for repeating the above separation with another and larger specimen of acetates which was purified as described above. After the mixture had been fractionated and each fraction again purified, the resulting esters, which melted in the case of the lowest indefinitely at 0° and the highest at 9°, were converted into alcohols and repeatedly recrystallised from acetone followed by benzene until substances of constant melting point were obtained. Three alcohols were isolated in quantity; the most fusible one melted at 59° (Found: C, 81·6; H, 14·2%), another fused at 63·4° (Found: C, 81·0; H, 14·3%), and the least soluble melted at 66·5° (Found: C, 82·0; H, 14·4%). These alcohols are snow-white, microcrystalline powders, and the

crystals appear to belong to the hexagonal systems. An *X*-ray examination of these specimens will be published later.

Although there is but little doubt that these substances are not pure, yet the analyses again point very clearly to the presence of alcohols of similar carbon content to two of the hydrocarbons present in paraffin, *viz.*, $C_{24}H_{50}$ and $C_{25}H_{52}$. A very prolonged fractionation, probably similar to that required in the case of the hydrocarbons themselves, would be necessary before pure alcohols could be isolated.

In the fractionation of these acetates there was always a high-boiling residue which on analysis was shown to contain dioxy-substances.

4. *Nature of the Alcohols.*—The fractionation of the purified acetates had given a series of what we expected would prove to be primary alcohols (two only have been described above), and it was hoped that it would have been possible to examine these more fully in the form of their corresponding acids. They gave, however, no acids or evolution of hydrogen when heated with potash and potash lime (Hell reaction, *Annalen*, 1884, **223**, 269), and it was clear that the hydroxy-derivatives formed in the oxidation were secondary alcohols, since paraffin contains only *n*-hydrocarbons. The small yields and the difficulty with which phthalic acid esters were formed from the alcohols supported this conclusion.

The action of a series of oxidising agents on these alcohols was investigated, but the results did not warrant further work. If the acids resulted, they were obtained in small yield and of lower molecular magnitude than the alcohols used, or were gummy transparent materials difficult to investigate. One of the products of oxidation with potassium permanganate in acetic acid solution was isolated; it appeared to be identical with the dioxy-substance previously mentioned (Found: C, 79·3; H, 13·5%. The average analysis of the dioxy-material is C, 79·3; H, 13·7%).

5. *Separation of the Carbonyl Compounds.*—The method used in the isolation of the mixture of carbonyl compounds and hydrocarbons from the alcohols has been previously mentioned (section 3). These derivatives were obtained from the various fractions of alcohol-acetates, but those of higher boiling point could not be completely freed from acetates by the method described.

Three fractions were selected and boiled in alcoholic solution with hydroxylamine. The resulting oximes were separated from the hydrocarbons by taking advantage of their greater solubility in acetone, and purified by treatment with cold alcohol, in which they were readily soluble. The oximes were viscous oils and gave white, well-defined, crystalline ketones on hydrolysis. These

ketones showed no acetyl value and hence were free from alcohols, but we were unable to separate the diketones with which they were contaminated.

Three specimens of ketones prepared in this manner from different fractions were purified by crystallisation from acetone and gave the data mentioned below. In the first two cases, the ketones were reduced with sodium in amyl alcohol to the corresponding alcohols, for which analytical data are also given, and these alcohols were further converted into their liquid acetates, which were analysed. The data obtained were interpreted in conjunction with the results of *X*-ray analysis, a summary of which is given below.

1. *Ketone*, m. p. 51·5—53°. Found: C, 80·8; H, 13·9. $C_{26}H_{52}O$ requires C, 82·0; H, 13·8%.

Secondary alcohol, m. p. 51—52°. Found: C, 80·3; H, 14·1; acetyl value, 123; *M*, ebullioscopic in chloroform, 374. $C_{26}H_{54}O$ requires C, 81·6; H, 14·2%; acetyl value, 132; *M*, 382.

The acetate of the secondary alcohol. Found: C, 78·4; H, 13·6. $C_{28}H_{56}O_2$ requires C, 79·2; H, 13·3%.

2. *Ketone*, m. p. 57—58°. Found: C, 80·9; H, 13·8. $C_{28}H_{56}O$ requires C, 82·3; H, 13·8%.

Secondary alcohol, m. p. 59—60°. Found: C, 80·3; H, 14·1; acetyl value, 125; *M*, ebullioscopic in chloroform, 391. $C_{28}H_{58}O$ requires C, 81·8; H, 14·2%; acetyl value, 124; *M*, 410.

The acetate of the secondary alcohol. Found: C, 78·8; H, 13·4. $C_{30}H_{60}O_2$ requires C, 79·6; H, 13·4%.

3. *Ketone*, m. p. 58·5—59·6°. Found: C, 81·2; H, 13·6. $C_{29}H_{58}O$ requires C, 82·4; H, 13·8%.

The above data show that none of these ketones was pure and it is probable that they were all contaminated with diketones. When the alcohols mentioned above were heated with potash and potash lime, they were not converted into acids, and gave no evolution of hydrogen. There can be no doubt, therefore, that they were secondary alcohols, and that the carbonyl derivatives from which they were obtained were ketones. This view was supported by an *X*-ray examination of these derivatives for which our best thanks are due to Mr. S. H. Piper. The results of this analysis, which will be published in a later communication, showed that specimen 1 had certainly a carbon-chain length of 26 atoms with the ketonic oxygen atom three (or four) from the end, specimen 2 probably a chain of 28 carbons, and specimen 3 a chain of 29 atoms, in both cases the oxygen atom being probably situated on the third (or fourth) carbon atom. These ketones have the same carbon content as three *n*-hydrocarbons known to be present in the paraffin wax used in this investigation, *viz.*, $C_{26}H_{54}$, $C_{28}H_{58}$, $C_{29}H_{60}$.

6. *Dioxy-derivatives.*—The method used for the separation of the soluble mixture of dioxy-materials has been described in section 2. This mixture gave on analysis C, 79·8; H, 13·3%, and an acetyl value of approximately 100.

After acetylation and treatment of the resulting product with cold alcohol, about 7% of monoketones crystallised, and the residual brown oil gave on analysis C, 76·6; H, 12·6%; acetyl value, 100; *M*, 407 in chloroform, 413 in benzene. These data approximate to those required for an acetate $C_{26}H_{50}O_3$, *viz.*, C, 76·0; H, 12·3%; acetyl value, 137; *M*, 410. The low acetyl value, however, indicates that the main constituent of the mixture is a hydroxy-carbonyl derivative of about the same average carbon content as the paraffins which had been oxidised. No acidic material could be obtained from this substance by heating with potash lime at 300°.

We were unable to devise any satisfactory method for the separation of this mixture, although a partial one was effected by shaking it with five times its weight of cold methyl alcohol, and an examination was made of that fraction (55% of the total material) which was soluble in that solvent at 0°. These acetates formed an orange-coloured oil, of saponification value 143. On saponification, they gave waxes very soluble in all organic solvents. The acetates were fractionated four times in a vacuum of 1 mm.; the main bulk boiled between 190° and 270° and of the fractions obtained, three were investigated: (A) b. p. 190—200°, (B) 220—230°, (C) 230—245°. The residue contained tri- or poly-oxy-derivatives and was not further examined.

The lowest fraction (A) consisted largely of monoxy-substance. The alcohols obtained from it gave, by the phthalic acid ester method, an impure alcohol, $C_{22}H_{46}O$ (*M*, 326), the molecular weight of which in chloroform was 311 and in benzene 323. Its acetyl value was 173, whereas that calculated for the above alcohol is 152, an indication that the impurity present was a dihydroxy-alcohol.

The second fraction (B) gave on analysis C, 75·4; H, 12·1%; saponification value, 150. $C_{24}H_{46}O_3$ requires C, 75·3; H, 12·1%; saponification value, 146·7. In spite of the correspondence of these data, however, there was no doubt that the substance was a mixture. The saponified products from this material when treated by the phthalic acid ester method, gave an impure *ketonic alcohol* which on analysis gave C, 76·9; H, 13·1%; *M*, 347 in chloroform and 352 in benzene. $C_{24}H_{48}O_2$ requires C, 78·2; H, 13·1%; *M*, 368. The acetate obtained from this derivative gave C, 74·0; H, 12·1%; saponification value, 189. The acetate of a ketonic alcohol, $C_{26}H_{50}O_3$, requires C, 76·0; H, 12·3%; saponification value, 136·8.

The impurity present was probably dihydric alcohols. The third fraction (C) gave on analysis C, 75·3; H, 12·0%; saponification value, 155. On reduction with sodium in amyl alcohol the acetyl value of the resulting product was 215, again pointing to the presence of hydroxy-carbonyl derivatives.

We concluded that the mixture of dioxy-material was composed of hydroxy-ketones and dihydroxy-alcohols and diketones. It was clear that the large amount of time required to effect the complete separation of such a mixture, or indeed that of the mono-alcohols and ketones, would scarcely be commensurate with the results that might be obtained. If crystalline derivatives, however, of the various groups described could be prepared, then the methods we have outlined, coupled with the fractional crystallisation of such derivatives, would finally enable pure materials to be isolated from the various mixtures mentioned in this communication, with relative ease in the case of alcohols and ketones but with much greater difficulty in the others.

Since we now know that the paraffin wax under investigation, and probably all such paraffins, are composed of a mixture of *n*-hydrocarbons, it is proposed to study the oxidation products of one of the suitable synthetic *n*-hydrocarbons under the same conditions that we have employed in the case of paraffin; such an investigation should not present the great difficulties we have met with.

Summary.

The investigation of the very complex mixture of non-acidic substances found among the products of the air-oxidation of paraffin wax at 100° has shown the great difficulty involved in isolating pure materials.

The preliminary survey published by Grun, however, has been considerably extended and it has been established that secondary alcohols and ketones are present, and with less certainty dihydroxy-alcohols, hydroxy-ketones, and diketones. Primary alcohols, if formed at all, which appears unlikely, must pass immediately to acids, since they are not present in the partly oxidised wax.

These non-acidic products diminish in amount as the oxidation proceeds and are replaced by acids. It has been shown that the various secondary alcohols and ketones which were isolated have, in all probability, the same carbon content as six out of the seven normal hydrocarbons comprising the greater part of paraffin wax.

The ketones are derived from the secondary alcohols which are the primary products of the oxidation, and the point at which the carbon chain is attacked by oxygen was shown, by an *X*-ray examination of these ketones, to be the third (or fourth) atom from the end.

On further oxidation the ketones may break down to acids of smaller carbon content. In a later communication it will be shown that the highest acid formed in the oxidation has a carbon content of 28 atoms, whereas the highest hydrocarbon present in any quantity in paraffin is $C_{31}H_{64}$.

It is also possible that alcohols and ketones may be oxidised to dihydric alcohols, hydroxy-ketones, and diketones before the final stage of acids is reached.

Our thanks are due both to the Department of Scientific and Industrial Research for assistance which enabled one of us (H. F. G.) to take part in this investigation, and to the Colston Research Committee for grants towards the expenses of the work.

UNIVERSITY OF BRISTOL. [*Received, May 22nd*, 1926.]

CCCXVII.—*Studies in the Diphenyl Series. Part II. The Nitration of Diphthalylbenzidine.*

By HERBERT HENRY HODGSON.

CAIN and his co-workers (J., 1912, **101**, 2298) described the nitration of diphthalylbenzidine and concluded that the nitration products were 3 : 3′(?)-dinitrobenzidine, 2 : 2′-dinitrobenzidine, and a mononitrobenzidine. They also found (*loc. cit.*, p. 2302) that in the nitration of diacetylbenzidine some 3 : 3′(?)-dinitrobenzidine was formed.

Le Fèvre and Turner (this vol., p. 1760) have shown the supposed 3 : 3′-product to be actually the 2 : 3′-dinitrobenzidine, a conclusion also foreshadowed by the present author (this vol., p. 1756).

An explanation is still required, however, for the fact that the tetra-aminodiphenyl prepared from 2 : 3′-dinitrobenzidine was stated by Cain (*loc. cit.*, p. 2303) to give a diquinoxaline derivative identical with that prepared from Strakosch's 3 : 5′-dinitrobenzidine, a result supported much later by Brady and McHugh (J., 1923, **123**, 2047). The solution to this problem would appear to be that, in the nitration of diphthalylbenzidine, varying amounts of the 3 : 5′-dinitrobenzidine are formed in addition to the products cited above. Cain, and later Brady, could then have obtained the same diquinoxaline from the mixture of tetra-aminodiphenyls produced by reduction of the mixed dinitrobenzidines. Moreover, Brady and McHugh's detailed description (*loc. cit.*, p. 2052) strongly suggests that they were dealing with such mixtures.

To test this viewpoint, the mixture of dinitrodiphthalylbenzidines

was hydrolysed and the dinitrobenzidines were converted by Cain's method (J., 1913, **103**, 2082) into the corresponding mixture of di-iododinitrodiphenyls from which Cain's 4 : 4′-di-iodo-3 : 5′-dinitrodiphenyl was ultimately isolated, thereby establishing the formation of 3 : 5′-dinitrobenzidine in the nitration of diphthalylbenzidine.

Experimental.

For purposes of comparison the following di-iodonitrodiphenyls were prepared :

4 : 4′-*Di-iodo*-2-*nitrodiphenyl*. 2-Nitrobenzidine was diazotised in concentrated sulphuric acid, and, after removal of excess of nitrous acid, the diluted solution was added to one of potassium iodide. The product is moderately soluble in alcohol and glacial acetic acid, and sublimes readily in a vacuum giving light yellow needles, m. p. 156° (Found : N, 3·3; I, 55·9. $C_{12}H_7O_2NI_2$ requires N, 3·2; I, 56·3%).

4 : 4′-*Di-iodo*-2 : 2′-*dinitrodiphenyl*, prepared from 2 : 2′-dinitrobenzidine as above, sublimes slowly in a vacuum and crystallises from alcohol in light yellow needles, m. p. 188° (Found : N, 5·7; I, 51·0. $C_{12}H_6O_4N_2I_2$ requires N, 5·6; I, 51·2%).

4 : 4′-*Di-iodo*-2 : 3′-*dinitrodiphenyl*. The above 4 : 4′-di-iodo-2-nitrodiphenyl was dissolved in synthetic nitric acid, and the solution on cooling deposited crystals which were removed, washed, dried, and sublimed in a vacuum; slender, light yellow needles, m. p. 156—157° (Cain, *loc. cit.*, gives m. p. 151—152°) (Found : N, 5·7; I, 51·1. Calc. : N, 5·6; I, 51·2%); a mixture with 4 : 4′-di-iodo-2-nitrodiphenyl melted at 142°.

When 4 : 4′-di-iododiphenyl is nitrated similarly a mixture of mono- and di-nitro-products results.

4 : 4′-*Di-iodo*-3 : 5′-*dinitrodiphenyl* sublimes in parallelogram-shaped plates, m. p. 252° (Cain, *loc. cit.*, gives 252—253°) (Found : N, 5·5; I, 51·0. Calc. : N, 5·6; I, 51·2%).

Nitration of Diphthalylbenzidine.—This was carried out by careful addition of the finely-powdered solid to ten times its weight of synthetic nitric acid. Two sets of experiments were made : (*a*) at 0°; (*b*) allowing the temperature to rise 40—50° owing to the heat of reaction.

Contrary to Cain's statement (*loc. cit.*, p. 2303), scarcely any hydrolysis occurs on pouring the product into water, and to effect this operation the mixture of dried dinitrodiphthalylbenzidines was hydrolysed by treating with eight times its weight of concentrated sulphuric acid at 130° for 20 minutes, then pouring into twenty times its weight of water, the precipitate being filtered

off, dried, and again subjected to the acid process. The united filtrates were precipitated by ammonia, and all the solids extracted with warm dilute alkali to effect removal of phthalic acid or anhydride.

The product of cold nitration (*a*) always yielded a greater portion soluble in warm dilute sulphuric acid and its m. p. was always lower (190—200°). Cain (*loc. cit.*, p. 2303) has shown this product to be mainly a mixture of 2 : 2′- (m. p. 214°) and 2 : 3′-dinitrobenzidines with, probably, a mononitrobenzidine. This was now substantiated by conversion of the product into a mixture of di-iodonitrodiphenyls which melted below 150° and possessed a nitrogen content between the values required for 4 : 4′-di-iodo-mono- and -di-nitrodiphenyls.

The products insoluble in dilute sulphuric acid were diazotised in concentrated sulphuric acid solution and converted into iodo-compounds as above. On analysis, all proved to be mixtures of 4 : 4′-di-iododinitrodiphenyls. The latter were repeatedly extracted with boiling alcohol, and the extracts on cooling deposited microcrystalline products of m. p.'s at first *ca.* 200° but later below 150°. The residues had m. p.'s above 200° and, after crystallisation from glacial acetic acid, these were raised to 240°. The latter products slowly sublimed when heated in a vacuum, giving parallelogram-shaped plates of m. p. 252°, identical with Cain's 4 : 4′-di-iodo-3 : 5′-dinitrodiphenyl (Found: N, 5·7; I, 49·9. Calc.: N, 5·6; I, 51·2%). This product was present in much greater amount in the warm nitration mixture (*b*).

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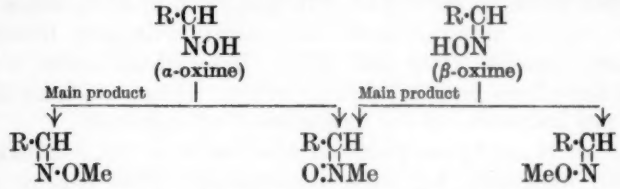
CCCXVIII.—*The Isomerism of the Oximes. Part XXVI. The Methyl Ethers of the Aldoximes.*

By OSCAR L. BRADY, FREDERICK P. DUNN, and RICHARD F. GOLDSTEIN.

DESPITE the importance attaching to the alkyl derivatives in connexion with the theories of oxime isomerism, little experimental work has been done on the methylation of the aldoximes since that of the early investigators of this subject (Gabriel and Meyer, *Ber.*, 1881, **14**, 2337; Gabriel, *Ber.*, 1882, **15**, 3067; Petraczek, *Ber.*, 1883, **16**, 826; Goldschmidt and co-workers, *Ber.*, 1890, **23**, 2163; 1891, **24**, 2548, 2808; 1893, **26**, 2103).

Werner ("Lehrbuch der Stereochemie," 1904, p. 277) states clearly that on methylation the α-aldoximes give mainly the *O*-ether

with some *N*-ether, and the β-aldoximes mainly the same *N*-ether as that obtained from the α-aldoxime and some of the isomeric *O*-ether. Adopting the new configuration (Brady and Bishop, J., 1925, **127**, 1357), this statement may be represented diagrammatically thus :



Werner also says that different oximes give different proportions of the two ethers; he gives, however, no references to the experimental work on which these views were founded, but our own experience soon confirmed their correctness (Brady, J., 1914, **105**, 2108, 2110). Although Goldschmidt and Zanoli (*Ber.*, 1892, **25**, 2587) observed that α-furfuraldoxime gave both the *O*- and the *N*-ether on methylation, and Beckmann (*Ber.*, 1889, **22**, 1535) was aware that two ethers were formed in the alkylation of α-oximes, yet Goldschmidt (*Z. Elektrochem.*, 1908, **14**, 581), in his work on the velocity of methylation of the sodium salts of α-aldoximes, seems to have considered either that no *N*-ether was formed or that it was formed in such small quantities as not to influence his results. The solubility of the *N*-ethers in water and their sparing solubility in ether are the probable reasons for their formation having been overlooked; for example, the distribution coefficient of *N*-methyl-3 : 4-methylenedioxybenzaldoxime between ether and water is 1 : 7. They can, however, be extracted from aqueous solutions by chloroform.

The stereochemical hypothesis demands two isomeric *N*-ethers from unsymmetrical oximes and, although two have been obtained from certain ketoximes (Semper and Lichtenstadt, *Ber.*, 1918, **51**, 928; Plowman and Whiteley, J., 1924, **125**, 587; Brady and Mehta, *ibid.*, p. 2297), yet it is remarkable that there is no example of a pair of isomeric *N*-ethers of any aldoxime (compare Goldschmidt and Zanoli, *loc. cit.*; Scheiber, *Annalen*, 1909, **356**, 215).

This communication forms the first part of a detailed study of the methyl ethers of the aromatic aldoximes; the main problems that have been considered are : (1) a search for the second *N*-ether, (2) the best method of preparing the β-*O*-ethers, and (3) a qualitative (and roughly quantitative) investigation of the products of methylation of the aldoximes under various conditions, as a preliminary to more accurate quantitative measurements.

No evidence has been obtained of the existence of a second

N-ether, although twelve of these compounds have been prepared by the methylation of the α- and β-oximes with methyl iodide and methyl sulphate under differing conditions, and by the action of β-methylhydroxylamine on the aldehydes. This last method of preparation seems to have been little employed in cases where the *N*-ethers can be obtained from the β-oxime (compare, however, Beckmann, *Annalen*, 1909, **365**, 208). The hydrochlorides of the *N*-ethers have been prepared and the ethers regenerated from them without any indication of the formation of an isomeride.

The action of methyl sulphate on solutions of α- and β-aldoximes in sodium hydroxide has been investigated. This reagent was used by Ponzio and Charrier (*Gazzetta*, 1907, **37**, i, 508), who isolated only the *O*-ether from α-benzaldoxime and α-*p*-methoxybenzaldoxime; indeed, they recommend this reagent as giving the *O*- and not the *N*-ether in the case of acetaldoxime (compare Dunstan and Goulding, J., 1901, **79**, 635). Ponzio and Charrier state that they obtained crystalline chloroplatinates from their *O*-ethers, a result we have been unable to confirm; moreover, it seems very unlikely that such compounds would be formed, since all attempts to obtain hydrochlorides of *O*-ethers have been unsuccessful, these compounds being, apparently, devoid of basic properties; on the other hand, the *N*-ethers form chloroplatinates and it seems that Ponzio and Charrier's supposed pure *O*-ethers contained some *N*-ether.

Our methylations of the α-aldoximes have been carried out by dissolving 1 equiv. of the oxime in $1\frac{1}{6}$ equivs. of 2*N*-sodium hydroxide, and shaking at room temperature with slightly more than 1 equiv. of methyl sulphate. Under these conditions, considerable quantities of *N*-ether are formed—in some cases as much as 40% of the total yield of ethers. Ponzio and Charrier's method, using 30% sodium hydroxide, would give a smaller proportion of *N*-ether, as will be shown in a subsequent paper.

The large amount of *N*-ether formed eliminates the possible explanation that the so-called α-oximes are equilibrium mixtures of the two isomerides (compare Cameron, *J. Physical Chem.*, 1898, **2**, 409), since, if the β-isomeride was present in so great an amount, it would be impossible to overlook the nitrile which would inevitably be formed on treatment with acetic anhydride and alkali; moreover, the *N*-ether is obtained in fair quantity from oximes which are known only in one form, *e.g.*, from *o*-methoxybenzaldoxime.

A few experiments have been made on the methylation of the α-aldoximes with methyl iodide in methyl alcohol in the presence of sodium methylate, and here again the *N*- in addition to the *O*-ether is formed.

When the α-aldoximes are dissolved or suspended in methyl iodide or methyl sulphate and kept in the dark for some time, in many cases they are converted into the hydriodides or methosulphates of the *N*-methyl ethers, no trace of the *O*-compounds being formed. These salts on decomposition with sodium carbonate give the same *N*-methyl derivative as is obtained by the other methods of preparation. Luxmoore (J., 1896, **69**, 183) thought he had obtained a second *N*-ether from the hydrobromide of *N*-methyl benzaldoxime, but it was ultimately shown to be a hydrate (Scheiber, *loc. cit.*); we have had similar experiences.

The exclusive formation of *N*-ether in non-ionising media, and the proportions of *N*-ether formed by methylation of different oximes in sodium hydroxide solution with methyl sulphate, suggested that the relative amounts of the two ethers formed bore some relation to the dissociation constants of the oximes—the more acidic the oxime the smaller the amount of *N*-ether formed. Further evidence for this view will be brought forward in a subsequent communication.

The β-*O*-methyl ethers have previously been obtained by the action of methyl iodide on the dry silver salts of the β-oximes; this preparation is troublesome, but we have found that good results are obtained by boiling the β-oxime under reflux with methyl iodide, ether, and dry silver oxide. β-O-*Methyl*-m-*nitro*-p-*methoxybenzaldoxime* has been obtained by this method as a crystalline solid, this being the third case where both *O*-methyl ethers of an aldoxime have been definitely characterised.

Experimental.

The Action of β-Methylhydroxylamine on Aldehydes.

Various methods of preparation have been employed, partly with the object of ascertaining whether variation of procedure would give the second *N*-ether, and partly owing to the different properties of the aldehydes and *N*-ethers.

(1) 3 : 4-*Methylenedioxybenzaldehyde.*—(*a*) The aldehyde (5 g.), dissolved in the minimum amount of alcohol, was mixed with β-methylhydroxylamine hydrochloride (2·75 g.), also in the minimum of alcohol, and a solution of sodium (0·76 g.) in alcohol added. After being kept over-night, the alcohol was removed on the water-bath and the residue extracted three times with boiling benzene. Most of the solvent was removed on the water-bath and the remainder evaporated at room temperature in a current of air. On crystallising the solid from benzene–light petroleum, there separated colourless plates of N-*methyl*-3 : 4-*methylenedioxybenzaldoxime hydrate*, m. p. 77°, which lost water on keeping for 48 hours over solid sodium hydroxide (Found : N, 7·4; H_2O, 9·4. $C_9H_9O_3N,H_2O$ requires

N, 7·1; H_2O, 9·1%). N-*Methyl*-3 : 4-*methylenedioxybenzaldoxime* crystallises from benzene in colourless plates, m. p. 108° (Found: N, 7·9. $C_9H_9O_3N$ requires N, 7·8%).

(*b*) The following was a quicker method: The aldehyde (16 g.) was just melted under water (50 c.c.) and β-methylhydroxylamine hydrochloride (10 g. in 50 c.c. of water) added, followed by sodium hydroxide (5 g. in 25 c.c. of water). On shaking, the oil dissolved, and after a few minutes the hydrate of *N*-methyl-3 : 4-methylenedioxybenzaldoxime separated and was collected, washed with a very small quantity of water, and air-dried; yield 18 g. of crude product, m. p. 75—76°. From the filtrate and washings a further 2 g. were recovered by extracting twice with chloroform.

(2) *Benzaldehyde.*—The aldehyde (13 g.) was suspended in 2*N*-sodium hydroxide (70 c.c.) and β-methylhydroxylamine hydrochloride (11 g. in 25 c.c. of water) added. After shaking for 5 minutes, the aldehyde had disappeared; the *N*-methylbenzaldoxime remaining in solution was extracted four times with chloroform; after removal of the solvent on the water-bath, the residue solidified on cooling and scratching and was dried for some days over solid sodium hydroxide. On crystallising from benzene and light petroleum pure *N*-methylbenzaldoxime (m. p. 82°) was obtained in almost theoretical yield. The m. p. is given in the literature as 69—72° but this low value is probably due to the presence of hydrate, since we have found that, however prepared, the compound always has the higher m. p. when carefully purified and dried.

(3) p-*Nitrobenzaldehyde.*—(*a*) The aldehyde (9 g.) was dissolved in the minimum amount of hot alcohol and a solution of β-methylhydroxylamine hydrochloride (5 g.) in alcohol added; *N*-methyl-*p*-nitrobenzaldoxime began to crystallise at once. After the mixture had cooled, it was separated, washed with a little alcohol and air-dried, 8 g. of the pure compound (m. p. 208°) being obtained. A small quantity of the same compound, but less pure (m. p. 200—205°), was obtained by diluting the mother-liquors. The feeble basicity of *N*-methyl-*p*-nitrobenzaldoxime—its hydrochloride is very readily hydrolysed, see below—and its sparing solubility enable the aldehyde to react with β-methylhydroxylamine hydrochloride in the absence of alkali.

(*b*) A solution of β-methylhydroxylamine hydrochloride (2 g.) in alcohol was mixed with one of sodium (0·6 g.) in alcohol, the precipitated sodium chloride removed and the filtrate added to *p*-nitrobenzaldehyde (3·5 g.) dissolved in alcohol (60 c.c.) at 35°. The colour changed to green, then orange, and yellow crystals began to separate which were collected after 30 mins. and found to be *N*-methyl-*p*-nitrobenzaldoxime (m. p. 205°). The mother-

liquors were diluted and the precipitate (m. p. 160°) subjected to a careful fractional crystallisation, but only the ordinary *N*-ether and some unchanged *p*-nitrobenzaldehyde were recovered.

(4) 6-*Nitro*-3 : 4-*methylenedioxybenzaldehyde*.—Method (3*b*) was employed using 5 g. of aldehyde in 100 c.c. of warm alcohol, 5 g. of β-methylhydroxylamine hydrochloride and 0·7 g. of sodium. N-*Methyl*-6-*nitro*-3 : 4-*methylenedioxybenzaldoxime* crystallises from hot water or from alcohol in deep yellow, dichroic needles, m. p. 210° (decomp.) (Found : N, 12·8. $C_9H_8O_5N_2$ requires N, 12·5%).

(5) 3 : 4-*Dimethoxybenzaldehyde*.—Method (1*a*) was employed, using 4 g. of aldehyde in 20 c.c. of alcohol, 2·5 g. of β-methylhydroxylamine hydrochloride, and 0·7 g. of sodium. On cooling the benzene extract, the *N*-ether crystallised in good yield; after recrystallising from benzene, N-*methyl*-3 : 4-*dimethoxybenzaldoxime* was obtained in faintly pink leaflets, m. p. 127° (Found : N, 7·5. $C_{10}H_{13}O_3N$ requires N, 7·2%).

(6) o-*Methoxybenzaldehyde*.—Method (1*a*) was employed, using 6 g. of aldehyde in 15 c.c. of alcohol, 4 g. of β-methylhydroxylamine hydrochloride, and 1·1 g. of sodium. The benzene extract, on concentrating and scratching, deposited crystals which, after crystallising from benzene–light petroleum, gave N-*methyl*-o-*methoxybenzaldoxime* in felted masses of long, white needles, m. p. 85° (Found : N, 8·7. $C_9H_{11}O_2N$ requires N, 8·5%). When this compound was dissolved in a very small quantity of hot water and the solution cooled in a freezing mixture, a *hydrate* separated, m. p. 27—28°; this loses water very readily and it was found impossible to determine its composition; after pressing on a porous tile, the loss in weight on drying over sodium hydroxide varied between 21 and 40%. The compound, therefore, probably contains more than one mol. of water of crystallisation.

(7) p-*Chlorobenzaldehyde*.—Method (1*a*) was employed, using 5 g. of aldehyde, 5 g. of β-methylhydroxylamine hydrochloride and 0·9 g. of sodium, and extracting with hot chloroform instead of with benzene. After crystallising twice from benzene, N-*methyl*-p-*chlorobenzaldoxime* was obtained in colourless plates, m. p. 128° (Found : N, 8·5. C_8H_8ONCl requires N, 8·3%).

(8) o-*Nitrobenzaldehyde*.—The aldehyde (7 g.) in warm alcohol (25 c.c.) was mixed with β-methylhydroxylamine hydrochloride (4·5 g.) in the minimum amount of water, and a concentrated aqueous solution of potassium acetate (5 g.) added. After 2 hours, excess of water was added and the solution extracted twice with chloroform. The extract on evaporation gave an oil which solidified on seeding; after crystallisation from benzene–light petroleum, 5 g. of *N*-methyl-*o*-nitrobenzaldoxime were obtained;

m. p. 92°. Occasionally this compound crystallised in a mixture of two forms, long needles and plates; after separation by hand, both forms melted at 92°, and a mixture at the same temperature.

(9) m-*Nitrobenzaldehyde*.—(*a*) Method (8) was employed, using 7 g. of aldehyde in 25 c.c. of warm alcohol, 4·5 g. of β-methylhydroxylamine hydrochloride and 5 g. of potassium acetate. The dilution of the mixture with water resulted in the precipitation of *N*-methyl-*m*-nitrobenzaldoxime (m. p. 110—114°) which was collected and then washed with a small quantity of water; the filtrate and washings on extraction with chloroform gave a further quantity of *N*-ether. One crystallisation from benzene–light petroleum gave the pure compound (m. p. 118—119°) in each case. Method (3*b*) was also used, but the same *N*-ether was obtained.

(*b*) The aldehyde (15 g.) and β-methylhydroxylamine hydrochloride (10 g.) in alcohol (100 c.c.) were warmed for 2 hours at 50° (compare Beckmann, *Annalen*, 1909, **365**, 201). On dilution with water, an oil and a solid were obtained which were taken up with ether; on removing the ether at room temperature, an oil and a solid remained; they were filtered at the pump, and the solid was washed with a little ether; a crude *N*-methyl-*m*-nitrobenzaldoxime (m. p. 97°) remained, which after one crystallisation from benzene gave the pure compound. The filtrate and ether washings on evaporation gave an oil from which *m*-nitrobenzaldehyde slowly crystallised. The oily residue was dissolved in ether and saturated with hydrogen chloride; the precipitate, on decomposition with sodium carbonate, gave the ordinary *N*-methyl ether, and the ethereal solution on evaporation yielded *m*-nitrobenzaldehyde. In this case, the reaction was incomplete, but no indication of the formation of a new *N*-ether was obtained.

When *N*-methyl-*m*-nitrobenzaldoxime is crystallised from hot benzene, it separates in long, fine needles; if these are left for some weeks in contact with the mother-liquor, the bulky crystals slowly disappear and are replaced by compact, rhombic crystals; both forms have the same m. p. alone or mixed.

(10) p-*Methoxybenzaldehyde*.—Method (2) was employed, using the same quantities but shaking for 30 minutes. After removing the chloroform, the oil was kept in an evacuated desiccator over solid sodium hydroxide for 24 hours and it then solidified on seeding. Crystallisation from light petroleum gave the pure *N*-ether, m. p. 76°. This compound is particularly troublesome to crystallise and light petroleum is the only solvent which gives satisfactory results, although it dissolves but little; the compound absorbs moisture from the atmosphere to form the monohydrate (m. p. 45°), and this crystallises unchanged from light petroleum; the

water is, however, lost on keeping for some time in a vacuum over solid sodium hydroxide.

(11) *Cinnamaldehyde.*—Method (1*a*) was employed, using 5 g. of aldehyde, 3·5 g. of β-methylhydroxylamine hydrochloride, and 0·95 g. of sodium. After removing most of the alcohol, the mixture was diluted with water, a tarry product filtered off, and the solution extracted twice with chloroform. On removing the solvent, a brown oil was obtained which solidified after 24 hours; it was pressed on a porous tile and crystallised from light petroleum containing a very little benzene; N-*methylcinnamaldoxime* separated in yellow needles, m. p. 87° (Found: N, 9·0. $C_{10}H_{11}ON$ requires N, 8·7%).

(12) 2 : 4-*Dinitrobenzaldehyde.*—Method (3*a*) was employed, using 2 g. of aldehyde in 3 c.c. of hot alcohol and 1 g. of β-methylhydroxylamine hydrochloride in 3 c.c. of alcohol. On mixing, heat was developed and after 30 minutes the yellow, crystalline precipitate was collected and crystallised from toluene, giving N-*methyl*-2 : 4-*dinitrobenzaldoxime*, yellow needles, m. p. 136° (Found: N, 18·9. $C_8H_7O_5N_3$ requires N, 18·7%).

With the exception of those containing nitro-groups, all the above *N*-ethers are readily soluble in water.

Hydrochlorides of N-*Ethers of Aldoximes.*

A solution of the *N*-ether in dry ether (or, in the case of those of *p*-nitro- and 6-nitro-3 : 4-methylenedioxy-benzaldoximes, in chloroform) was saturated with dry hydrogen chloride and the hydrochloride was immediately precipitated; this was collected, dried on a porous tile, the m. p. determined, a portion weighed and decomposed with 2*N*-sodium hydroxide for a halogen determination, and the rest decomposed with 2*N*-sodium carbonate solution. In all experiments of this type these operations were carried out as rapidly as possible. In the cases of *N*-methyl-*o*-, -*m*-, and -*p*-nitro- and -6-nitro-3 : 4-methylenedioxy-benzaldoximes, the precipitated solid obtained by treatment with sodium carbonate was found to be identical with the original *N*-ether by the method of mixed m. p.'s. If the minimum quantity of sodium carbonate solution was employed, *N*-methyl-*o*-methoxy- and -3 : 4-methylenedioxy-benzaldoximes separated in the hydrated form which, on keeping for a short time in a vacuum over solid sodium hydroxide, gave the original anhydrous compound. With *N*-methylbenzaldoxime and *N*-methyl-*p*-methoxybenzaldoxime, the soluble *N*-ethers were extracted from the sodium carbonate solution with chloroform, and the original *N*-ethers recovered by evaporation. Precipitation of the hydrochlorides from hot benzene solutions of the *N*-ethers

gave similar results (compare Brady and Dunn, J., 1923, **123**, 1783).

The following hydrochlorides were prepared:

N-*Methyl*-o-*nitrobenzaldoxime hydrochloride*, a pale yellow, crystalline powder, m. p. 125—134° (decomp.) (Found: Cl, 16·8. $C_8H_9O_3N_2Cl$ requires Cl, 16·4%); N-*methyl*-m-*nitrobenzaldoxime hydrochloride*, a white, crystalline powder, m. p. 172—177° (decomp.) (Found: Cl, 16·9. $C_8H_9O_3N_2Cl$ requires Cl, 16·4%); N-*methyl*-p-*nitrobenzaldoxime hydrochloride*, a white, crystalline powder, m. p. 133—135° (decomp.) (Found: Cl, 14·7. $C_8H_9O_3N_2Cl$ requires Cl, 16·4%) [The low value for chlorine is due to the instability of this compound, which rapidly loses hydrogen chloride, turning to the yellow colour of the free *N*-ether; it is at once decomposed by water.]; N-*methylbenzaldoxime hydrochloride*, a white, crystalline powder, m. p. 131—136° (decomp. at 171°) (Found: Cl, 20·6. $C_8H_{10}ONCl$ requires Cl, 20·7%); on keeping in air, decomposition occurs and the odour of benzaldehyde soon becomes apparent; N-*methyl*-3 : 4-*methylenedioxybenzaldoxime hydrochloride*, a pale yellow, crystalline powder, m. p. 176—180° (decomp.) (Found: Cl, 16·9. $C_9H_{10}O_3NCl$ requires Cl, 16·5%); N-*methyl*-o-*methoxybenzaldoxime hydrochloride*, a white, crystalline powder, m. p. 70—100° (decomp. at 151°) (Found: Cl, 17·5. $C_9H_{12}O_2NCl$ requires Cl, 17·6%); N-*methyl*-p-*methoxybenzaldoxime hydrochloride*, a white, crystalline powder, m. p. 175—179° (decomp.) (Found: Cl, 18·2. $C_9H_{12}O_2NCl$ requires Cl, 17·6%); N-*methyl*-6-*nitro*-3 : 4-*methylenedioxybenzaldoxime hydrochloride*, a pale yellow, crystalline powder, m. p. 173—175° (decomp.) (Found: Cl, 13·7. $C_9H_9O_5N_2Cl$ requires Cl, 13·6%).

Action of Methyl Sulphate on Aldoximes.

Methyl sulphate (10 c.c.) and finely-powdered α-*o*-nitrobenzaldoxime (5 g.) were kept in a stoppered bottle in the dark for 8 months; a clear yellow solution was then obtained. Ether precipitated a yellow oil which solidified on cooling in a freezing mixture and scratching. After collecting, washing with dry ether, and drying between filter-paper, N-*methyl*-o-*nitrobenzaldoxime methosulphate* was obtained in practically theoretical yield as a pale yellow, crystalline powder, m. p. 99—107° (Found: N, 9·5; SO_4, 33·1. $C_9H_{12}O_7N_2S$ requires N, 9·6; SO_4, 32·9%). The methosulphate dissolved in 2*N*-sodium carbonate with evolution of carbon dioxide and separation of a yellow solid, which was found to be *N*-methyl-*o*-nitrobenzaldoxime; the alkaline solution, on digestion with concentrated hydrochloric acid and distillation, gave methyl alcohol, identified by oxidation to formaldehyde. N-*Methyl*-m-

nitrobenzaldoxime methosulphate, prepared in good yield similarly to the above, was a yellow, crystalline powder, m. p. 58—60° (Found: N, 9·0. $C_9H_{12}O_7N_2S$ requires N, 9·6%). α-*p*-Nitrobenzaldoxime slowly dissolves in methyl sulphate and bright yellow crystals of N-*methyl*-p-*nitrobenzaldoxime methosulphate* separate; m. p., after washing with ether, 85—91° (Found: N, 9·1. $C_9H_{12}O_7N_2S$ requires N, 9·6%). When both the *m*- and *p*-compounds are decomposed with 2*N*-sodium carbonate, the practically pure *N*-ether is precipitated. With α-benzaldoxime and methyl sulphate, colourless needles separated which, after collecting, washing with ether, and drying over solid sodium hydroxide, gave N-*methylbenzaldoxime methosulphate*, m. p. 60—63° (Found: N, 5·8. $C_9H_{13}O_5NS$ requires N, 5·7%). Treatment of this compound with sodium carbonate and extraction of the solution with chloroform gave *N*-methylbenzaldoxime; no trace of the characteristic odour of *O*-methylbenzaldoxime was observed in the mother-liquors from the methosulphate. α-*p*-Methoxybenzaldoxime dissolved slowly in methyl sulphate, and from the solution ether precipitated an oil which solidified only after a considerable time on scratching in a freezing mixture. After grinding the solid with ether and filtering, N-*methyl*-p-*methoxybenzaldoxime methosulphate* was obtained in good yield; white crystals, m. p. 89—90° (Found: N, 5·1. $C_{10}H_{15}O_6NS$ requires N, 5·1%). α-3 : 4-Methylenedioxybenzaldoxime slowly dissolved in methyl sulphate and large, colourless crystals separated; the mother-liquor went very dark owing, probably, to slight decomposition of the methylenedioxy-group. After collecting the solid and purifying by grinding with ether, an almost quantitative yield of N-*methyl*-3 : 4-*methylenedioxybenzaldoxime methosulphate* was obtained as colourless needles, m. p. 97—100° (Found: N, 4·9. $C_{10}H_{13}O_7NS$ requires N, 4·8%). In the last two cases, the corresponding *N*-ether was obtained by decomposing the methosulphates with sodium carbonate solution and extracting with chloroform. In the above results the reaction mixture was kept for 8 months, but decreasingly satisfactory yields were obtained in shorter times, and it was then necessary to precipitate the methosulphate with ether. The methyl sulphate must be free from acid; a sufficiently pure material can be obtained by shaking the commercial compound with two portions of 2*N*-sodium hydroxide for a minute, then with a little water, and drying with anhydrous potassium carbonate; distillation is not necessary.

Action of Methyl Iodide on α-Aldoximes.

(1) α-*Benzaldoxime.*—(*a*) The oxime (1 g.) was melted and mixed with methyl iodide (5 c.c.) and kept in a stoppered bottle in the

dark for 5 months. The brown crystals which had separated were collected, pressed on a porous tile, and washed with ether; they shrivelled at 65° and melted at 103°. On addition of 2*N*-sodium carbonate, carbon dioxide was evolved and the solution (after treatment with a few drops of sulphurous acid to remove iodine, and extraction with chloroform) gave 0·35 g. of *N*-methylbenzaldoxime, identified by a mixed m. p. and by hydrolysis. The remaining methyl iodide on evaporation gave no trace of the strong characteristic odour of *O*-methylbenzaldoxime.

(*b*) The oxime (5 g.) and methyl iodide (10 c.c.) were kept in the dark for 42 days; no crystals having separated, the brown solution was added to excess of ether, whereupon a brown solid separated, which was pressed on a porous tile and washed with ether, m. p. 73°; washing with acetone dissolved most of it, but a white solid remained which was apparently *N*-methylbenzaldoxime hydriodide: this darkened at 135° and melted at 150°; it was evidently impure (Found: I, 38·2. $C_8H_{10}ONI$ requires I, 48·3%). Carbon dioxide was liberated when this compound was treated with 2*N*-sodium carbonate, and chloroform extracted from the solution *N*-methylbenzaldoxime which was obtained pure on removing the solvent. On evaporating the ether–methyl iodide mixture, the odour of *O*-methylbenzaldoxime was absent.

(2) α-p-*Methoxybenzaldoxime*.—The finely-powdered oxime (5 g.) was added to methyl iodide (10 c.c.) and kept in a stoppered bottle in the dark for 28 days. The oxime slowly dissolved and was replaced by brownish needles of impure *N-methyl-p-methoxybenzaldoxime hydriodide* which, after being pressed on a porous tile and washed with ether, sintered at 131° and melted at 145° (Found: I, 30·5. $C_9H_{12}O_2NI$ requires I, 43·3%). Decomposition with sodium carbonate as with the previous compound, gave, on removing the chloroform, an oil from which crystals of *N*-methyl-*p*-methoxybenzaldoxime slowly separated; the residual oil contained *p*-methoxybenzaldehyde, due to partial hydrolysis of the *N*-ether—a common experience with this particular compound. In a second experiment, the brown solid was washed with acetone and a white, crystalline material remained, m. p. 155—159° (Found: I, 29·1%), whilst in a third similar experiment the product had m. p. 160° and appeared to be a *compound* of 2 mols. of the *N*-ether and 1 mol. of hydrogen iodide (Found: N, 6·7; I, 28·4. $2C_9H_{11}O_2N,HI$ requires N, 6·1; I, 27·7%). A determination of the amount of β-methylhydroxylamine formed on hydrolysis of this compound with hydrochloric acid gave 20·1% (Calc., 20·0%). The product on reaction with sodium carbonate gave *N*-methyl-*p*-methoxybenzaldoxime in a fairly pure condition. Again no indication of the

presence of the characteristic odour of *O*-methyl-*p*-methoxybenzaldoxime was observed from the methyl iodide mother-liquors in any of the experiments.

(3) α-o-*Methoxybenzaldoxime*.—The oxime (2 g.) in methyl iodide (10 c.c.) was kept as before for 25 days; it slowly dissolved and was replaced by long clusters of yellow needles with some darker crystals; these were collected, washed with ether, and the dark brown crystals removed by hand. The lighter-coloured product, m. p. 137° (Found: I, 41·7%), with sodium carbonate, as before, gave *N*-methyl-*o*-methoxybenzaldoxime. The methyl iodide solution on evaporation yielded a considerable amount of unchanged oxime. A second preparation was kept for 11 months and the crystals were washed with ether and acetone, N-*methyl*-o-*methoxybenzaldoxime hydriodide* being obtained as a lemon-yellow, crystalline powder, m. p. 142° (decomp.) (Found: I, 42·3. $C_9H_{12}O_2NI$ requires I, 43·3%).

(4) β-*Cinnamaldoxime*.—The oxime (2 g.) in methyl iodide (5 c.c.) was kept for 5 weeks; it slowly dissolved and was replaced by light brown crystals of N-*methylcinnamaldoxime hydriodide*, which were washed with ether, m. p. 71—79° (Found: I, 41·3. $C_{10}H_{12}ONI$ requires I, 43·9%). On decomposition with sodium carbonate, *N*-methylcinnamaldoxime was formed.

No satisfactory method of crystallising these hydriodides has been discovered. No appreciable reaction occurred between methyl iodide and α-*m*-nitro-, -*p*-nitro-, and -3 : 4-methylenedioxy-benzaldoximes in 3 months.

Action of Methyl Sulphate on Solutions of α-Aldoximes in Sodium Hydroxide.

The following methylations were carried out under similar conditions with the view of obtaining some idea of the relative amounts of *O*- and *N*-ethers formed from various aldoximes. In some cases methylation was incomplete with the limited amount of methyl sulphate employed, and difficulties of manipulation frequently resulted in loss of material; this was particularly marked in the case of the *N*-ethers, since, owing to the presence of traces of acid or alkali, distillation in steam sometimes caused considerable hydrolysis. The weights of ethers recorded are of the crude products unless otherwise stated, but in every case the compounds were subsequently purified and their identity was established by mixed m. p.'s.

Method 1. α-*o*-Nitrobenzaldoxime (10 g.), dissolved in 2*N*-sodium hydroxide (35 c.c.), was shaken at 20—25° for 15 minutes with methyl sulphate (6 c.c.). The mixture was extracted four times

with chloroform, water (50 c.c.) was added to the extract, and the whole distilled in steam; after the chloroform had passed over, the *O*-ether solidified in the condenser and was melted out from time to time; at the end of 2 hours no more *O*-ether distilled. After separating the chloroform from the distillate, the aqueous layer was extracted with a further quantity of chloroform and evaporation of the combined extracts gave *O*-methyl-*o*-nitrobenzaldoxime (7·0 g.). Extraction of the solution in the flask gave *N*-methyl-*o*-nitrobenzaldoxime (1·9 g.). The mother-liquor from the methylation, after acidification and extraction with chloroform, gave the unmethylated oxime (1·0 g.). In a similar way, α-*m*-nitrobenzaldoxime gave 6·7 g. of *O*-methyl ether and 0·6 g. of *N*-methyl ether. If during the methylation the temperature is allowed to rise, or if the mixture is left for too long, the solution becomes reddish-brown, due to hydrolysis of the *N*-ether and reduction of the nitro-group by the alkaline β-methylhydroxylamine.

Equivalent quantities of α-*o*- and -*p*-methoxy-, -*p*-chloro-, and -3 : 4-methylenedioxy-benzaldoximes were methylated in a similar manner. 4·5 G. of α-*o*-methoxybenzaldoxime gave 3·3 g. of α-O-*methyl*-o-*methoxybenzaldoxime*, a pleasant-smelling, colourless oil, b. p. 241°/761 mm., 138—139°/25 mm. (Found: N, 8·4. $C_9H_{11}O_2N$ requires N, 8·5%), 1·4 g. of *N*-methyl ether, and 0·03 g. of unchanged oxime. 9·0 G. of α-*p*-methoxybenzaldoxime gave 5·9 g. of *O*-methyl ether, 2·3 g. of *N*-methyl ether, and 0·7 g. of unchanged oxime. 9·0 G. of α-*p*-chlorobenzaldoxime gave 7·5 g. of α-O-*methyl*-p-*chlorobenzaldoxime*, colourless needles, m. p. 28° (Found: N, 8·3. C_8H_8ONCl requires N, 8·3%), 1·3 g. of *N*-methyl ether, and 0·1 g. of unchanged oxime. 10 G. of α-3 : 4-methylenedioxybenzaldoxime gave 6 g. of *O*-methyl ether and 0·6 g. of *N*-methyl ether; the *O*-ether solidified slowly and, after pressing on a porous tile and crystallising from dilute alcohol, pure α-O-*methyl*-3 : 4-*methylenedioxybenzaldoxime* was obtained as white, nacreous plates, m. p. 37° (Found: N, 7·9. $C_9H_9O_3N$ requires N, 7·8%). A somewhat larger quantity of benzaldoxime was employed for methylation: 35 g. gave 16 g. of redistilled *O*-methyl ether and 7·2 g. of *N*-methyl ether.

In two cases, a somewhat different procedure had to be adopted owing to the insolubility of the sodium salts. α-*p*-Nitrobenzaldoxime (10 g.) was added to 2*N*-sodium hydroxide (25 c.c.); it dissolved, but the sodium salt soon crystallised; water was added (25 c.c.), and then methyl sulphate (6 c.c.); the liquid became very thick and could not be shaken, so a further 25 c.c. of sodium hydroxide and 50 c.c. of water were added. After 5 minutes, the mixture was filtered and the solid washed with water and distilled in

steam. From the distillate, 7·6 g. of practically pure *O*-methyl ether were obtained and the orange solution in the flask deposited 1·0 g. of nearly pure *N*-methyl ether on cooling. α-6-Nitro-3 : 4-methylenedioxybenzaldoxime (10 g.) was dissolved in dilute sodium hydroxide (75 c.c. of 2*N*; 250 c.c. of water) and methyl sulphate (8 c.c.) added; on shaking, a solid soon separated and was collected after 5 minutes, the filtrate (*A*) being preserved. The solid was divided into two parts, (*B*) and (*C*). (*B*) was distilled in steam and a crystalline solid slowly passed over, which on crystallising from alcohol gave α-O-*methyl*-6-*nitro*-3 : 4-*methylenedioxybenzaldoxime* in yellow needles, m. p. 147° (Found : N, 12·7. $C_9H_8O_5N_2$ requires N, 12·5%). After 6 hours' distillation, the solid remaining in the flask melted at 140—147° and one crystallisation gave the pure *O*-ether. The solid (*C*) was fractionally crystallised from alcohol and was found to consist almost entirely of *O*-ether, but a very small quantity of impure *N*-ether was isolated from the more soluble fractions. The filtrate (*A*) slowly deposited more *O*-ether, which was separated and the filtrate extracted with chloroform; on removing the solvent and crystallising the residue from alcohol, a small amount of *N*-ether was obtained.

Method 2. The methylation was carried out as before, but the reaction mixture was extracted several times with ether, and the extract, after drying with anhydrous sodium sulphate, was saturated with dry hydrogen chloride. The precipitated hydrochloride of the *N*-ether was decomposed with dilute sodium carbonate solution and the *N*-ether extracted with chloroform. The ethereal solution was washed with water and, on drying and evaporating, it gave the *O*-ether. 10 G. of α-*p*-methoxybenzaldoxime gave 5·9 g. of *O*-ether and 2·1 g. of *N*-ether; 10 g. of α-3 : 4-methylenedioxybenzaldoxime gave 7·7 g. of *O*-ether and 0·4 g. of *N*-ether; 10 g. of α-*m*-nitrobenzaldoxime gave 7 g. of *O*-ether and 1·1 g. of *N*-ether.

Action of Methyl Sulphate on Solutions of β-*Aldoximes in Sodium Hydroxide.*

Previous workers have shown that the methylation of the β-aldoximes in methyl alcohol with sodium methylate and methyl iodide gives mainly the *N*-ether. The use of methyl sulphate with a solution of the β-aldoxime in aqueous sodium hydroxide is not very satisfactory as a guide to the relative quantities of the two ethers formed; in some cases, the sodium salt crystallises out, and in others trouble is caused by the hydrolysis of the *N*-ether. In order to avoid the presence, after the reaction, of unchanged oxime, which, owing to its feeble acidity, would be extracted by solvents from the alkaline solution, some excess of methyl sulphate is desir-

able; unfortunately, any of this which may be undecomposed passes into the chloroform extract and is hydrolysed during the steam-distillation, the resulting acid then hydrolysing the *N*-ether.

β-m-*Nitrobenzaldoxime*.—The oxime (7·3 g.) in 2*N*-sodium hydroxide (35 c.c.) was treated in the same way as the α-oxime with methyl sulphate (6 c.c.); the ethers were extracted with chloroform and distilled in steam. From the distillate, 2·8 g. of β-*O*-methyl-*m*-nitrobenzaldoxime, m. p. 57°, were obtained, the low m. p. being probably due to contamination with *m*-nitrobenzaldehyde from the hydrolysis of the *N*-ether. The residue in the flask gave, on extraction with chloroform, 4·6 g. of *N*-methyl-*m*-nitrobenzaldoxime.

β-p-*Methoxybenzaldoxime*.—Chloroform extraction and distillation in steam resulted in much hydrolysis of the *N*-ether; the β-oxime (4·5 g.) in 2*N*-sodium hydroxide (75 c.c.) was therefore methylated with methyl sulphate (4·5 c.c.). The emulsion obtained was extracted with ether (25 c.c.), in which the *O*-methyl ether is readily soluble. The ethereal layer was treated as before in order to produce the hydrochloride of the *N*-ether; yield 0·32 g., corresponding to 0·26 g. of *N*-ether. The filtrate from the hydrochloride was neutralised by sodium carbonate and on evaporation gave 0·41 g. of α-*O*-methyl-*p*-methoxybenzaldoxime, formed from the β-*O*-methyl ether by the hydrogen chloride. The original aqueous layer from the ether-extraction was extracted repeatedly with chloroform and, on evaporating the solvent, 3·42 g. of *N*-ether were obtained. From 4·5 g. of β-oxime there were therefore isolated 3·68 g. of *N*-ether and 0·41 g. of *O*-ether.

β-3 : 4-*Methylenedioxybenzaldoxime*.—Steam distillation of the chloroform extract as before gave large quantities of the aldehyde, but satisfactory results were obtained by the following method: A solution of the oxime (5 g.) in 2*N*-sodium hydroxide (80 c.c.) was treated with methyl sulphate (5 c.c.), shaken, with cooling under the tap, for 15 minutes, and then cooled in ice; most of the *N*-ether crystallised out, and was collected, washed with a little ice-water and then with ether, in which the *O*-ether is readily but the *N*-ether sparingly soluble. The *N*-ether, after dehydration in a vacuum over calcium chloride, weighed 3·75 g. The filtrate and washings, both aqueous and ethereal, were mixed and extracted twice with 25 c.c. of ether. The extract on being subjected to the usual process yielded 0·05 g. of the hydrochloride of the *N*-ether, corresponding to 0·04 g. of *N*-ether itself. A further 0·62 g. of *N*-ether was obtained from the aqueous portion by extraction with chloroform; making a total yield of 4·4 g. of *N*-ether. The ethereal extract, after treatment with solid sodium carbonate (to remove acid) and evaporation, gave 0·34 g. of an oil consisting of the

α-*O*-ether mixed with a little aldehyde, the former being produced by the action of the hydrogen chloride on the β-*O*-ether.

The methylation of the β-oximes without isolation of the oxime gave interesting results. A solution of α-*m*-nitrobenzaldoxime (5 g.) in dry chloroform was saturated with dry hydrogen chloride, the precipitated hydrochloride collected, pressed on a porous plate until free from chloroform, dissolved as rapidly as possible in 150 c.c. of 2*N*-sodium hydroxide, and the solution shaken for some minutes with methyl sulphate (5 g.), cooling under the tap. The solid was separated, washed with a little water, and distilled in steam. From the distillate almost pure β-*O*-methyl-*m*-nitrobenzaldoxime (m. p. 71—74°) crystallised; as the pure compound has m. p. 74°, the m. p. of the product indicates that practically no α-*O*-ether was present and consequently that there was little α-*m*-nitrobenzaldoxime in the alkaline solution. It appears, therefore, that the presence of a considerable amount of the α- in the β-oxime obtained by decomposing the hydrochloride in the usual way is due to isomeric change occurring during manipulation subsequent to the decomposition of the hydrochloride rather than to the hydrochloride being a mixture. The residual solution in the flask deposited almost pure *N*-ether on cooling. The yield of *N*-ether was greater than that of *O*-ether.

The hydrochloride from α-*p*-nitrobenzaldoxime (6 g.), obtained as before, was dissolved in 2*N*-sodium hydroxide (200 c.c.) and treated with methyl sulphate (10 g.). On collecting the ethers formed, washing, and distilling in steam, the aqueous solution in the flask on cooling deposited 3·5 g. of nearly pure *N*-ether, and 0·3 g. of the β-*O*-ether (m. p. 69—70°) crystallised from the distillate. Fractionation of this ether gave two fractions of m. p. 70°, and a third, m. p. 69°. The m. p. of the pure β-*O*-methyl ether is 70°, but it is raised by admixture with the α-*O*-ether, so there is not the same criterion of purity as with the *m*-nitro-compound (compare Brady and Dunn, J., 1913, **103**, 1625), but it seems probable that the alkaline solution from the hydrochloride was practically free from the α-oxime. The purity of the β-oxime-forming hydrochlorides in the case of *m*- and *p*-nitrobenzaldoximes is in accordance with expectation, since it has been shown that in these cases the α-oxime-forming hydrochlorides are stable only at very low temperatures (Brady and Dunn, J., 1916, **109**, 680; 1923, **123**, 1798).

Action of Methyl Iodide and Sodium Methoxide on α-o-, -m-, *and* -p-*Nitrobenzaldoximes.*

The oxime (5 g.) was dissolved in methyl alcohol, a solution of sodium (1 g.) in methyl alcohol added followed by methyl iodide

(7 g.), and the mixture kept at room temperature for 3 days. Water was added and the precipitated yellow solid distilled in steam. From the distillate the *O*-methyl ethers crystallised almost pure; the liquor remaining in the flask was evaporated on the water-bath and the residue crystallised from alcohol, giving a small amount of pure *N*-ether in each case.

Action of Methyl Iodide and Silver Oxide on Aldoximes.

α-m-*Nitrobenzaldoxime*.—A mixture of the oxime (5 g.), dry silver oxide (10 g.), and methyl iodide (20 c.c.) was heated under reflux for 30 minutes; ether was added and, after filtering, the ether and excess of methyl iodide were removed by a current of dry air. The yellow residue was washed with cold 2*N*-sodium hydroxide, which dissolved any excess of oxime and the *N*-ether, and one crystallisation of the residue from dilute alcohol gave 3·8 g. of pure α-*O*-methyl-*m*-nitrobenzaldoxime; by extracting the alkaline washings with chloroform, 0·4 g. of *N*-methyl-*m*-nitrobenzaldoxime was obtained.

β-m-*Nitrobenzaldoxime*.—The oxime (6 g., m. p. 113—118°) and dry silver oxide (12 g.) were added to methyl iodide (40 c.c.) and considerable heat was evolved; after heating under reflux for 45 minutes, ether was added and the filtered solution evaporated in a current of air. The crude residue was extracted with hot light petroleum and from the extract 1·2 g. of pure β-*O*-methyl-*m*-nitrobenzaldoxime crystallised. The residue insoluble in the petroleum and the silver oxide and iodide residues were extracted with boiling benzene and on evaporating to small bulk 0·2 g. of pure *N*-methyl-*m*-nitrobenzaldoxime crystallised. In a second experiment, 2 g. of oxime gave 1·1 g. of pure β-*O*-ether and some *N*-ether.

β-3-*Nitro*-p-*methoxybenzaldoxime*.—The oxime (2 g.), dry silver oxide (4 g.), and methyl iodide (20 c.c.) were boiled under reflux for an hour; ether was added and, after filtering, the solution was evaporated in a current of air and the residue distilled in steam; the *O*-ether passed over slowly and crystallised in the distillate; recrystallisation from alcohol gave β-O-*methyl*-3-*nitro*-p-*methoxybenzaldoxime* as very pale yellow-green plates, m. p. 135° (Found: N, 13·7. $C_9H_{10}O_4N_2$ requires N, 13·3%). A mixture of about equal parts of this compound and α-*O*-methyl-3-nitro-*p*-methoxybenzaldoxime (m. p. 120°) had m. p. 103—110°. After hydrogen chloride had been passed into an ethereal solution of the β-*O*-ether, evaporation in a current of air showed that complete conversion to the α-*O*-methyl ether had occurred.

The Action of Alkalis on Methyl Ethers.

Boiling 2*N*-sodium hydroxide has no appreciable action on the *O*-methyl ethers; with the *N*-ethers of, *e.g.*, benzaldoxime or *p*-methoxybenzaldoxime, on gentle warming an oil began to separate and the odour of the aldehyde was obvious. After 5 minutes on the water-bath, the solution was cooled and extracted with ether; the aqueous solution immediately reduced cold Fehling's solution, indicating the presence of β-methylhydroxylamine; the ethereal solution was evaporated and the resulting oil treated with semicarbazide hydrochloride and sodium acetate, whereupon an amount of the semicarbazone of benzaldehyde or *p*-methoxybenzaldehyde was obtained corresponding approximately with the quantity of *N*-ether used. Where a nitro-group was present, *e.g.*, with *N*-methyl-*m*-nitrobenzaldoxime, tarry products were obtained, owing probably to the reducing action of the β-methylhydroxylamine liberated.

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CCCXIX.—*The Isomerism of the Oximes. Part XXVII. The Mechanism of Methylation of the Aldoximes.*

By OSCAR L. BRADY and RICHARD F. GOLDSTEIN.

In a previous paper (Brady, Dunn, and Goldstein, this vol., p. 2398), it was shown that, when the sodium salts of the α-aldoximes are methylated in alcoholic or aqueous solution, a mixture of *O*- and *N*-ethers was formed, the *O*-ether preponderating. Goldschmidt (*Z. Elektrochem.*, 1908, **14**, 581) studied the velocity of methylation by methyl iodide of the sodium salts of some α-aldoximes in alcoholic solution. He concluded that the α-*O*-ethers were produced by a bimolecular reaction between the ion of the oxime and methyl iodide, $R{\cdot}CH{:}NO' + CH_3I \rightarrow (R{\cdot}CH{:}NO')(CH_3I) \rightarrow R{\cdot}CH{:}N{\cdot}OCH_3 + I'$. Further, he found that the methylation of the β-aldoxime sodium salts, in which the *N*-ether is the main product, also proceeded as a bimolecular reaction for which a similar mechanism was assumed:

$$R{\cdot}CH{:}NO' + CH_3I \longrightarrow \begin{matrix} R{\cdot}CH{:}NO' \\ CH_3 \diagup \diagdown I \end{matrix} \longrightarrow \begin{matrix} R{\cdot}CH{:}N{:}O \\ | \\ CH_3 \end{matrix} + I'.$$

Both these assumptions are open to question, since Goldschmidt overlooked the production of a considerable amount of *N*-ether in the methylation of α-aldoximes. Our work on this subject (Brady, Dunn, and Goldstein, *loc. cit.*) suggested that there was a relation between the amount of *O*-ether formed and the degree of dissociation of the sodium salt of the oxime, and a quantitative study of the methylation of a number of α-aldoximes has now been made.

The method consisted in dissolving the oxime in aqueous sodium hydroxide and methylating at room temperature with methyl sulphate. The products were removed by extraction with chloroform, and the unchanged oxime was determined in the aqueous portion, so that the amount of oxime actually methylated was known. In the estimation of the products of methylation, advantage was taken of the non-reactivity of the *O*-ethers; the chloroform was removed and the mixed methyl ethers were boiled with concentrated hydrochloric acid for a short time, whereby the *N*-ether was completely hydrolysed to aldehyde and β-methylhydroxylamine hydrochloride, leaving the *O*-ether unchanged. The aldehyde and *O*-ether were removed by extraction and the β-methylhydroxylamine was determined in the aqueous portion by a specially devised iodometric method.

The amounts of *O*- and *N*-methyl ethers formed on methylating several substituted benzaldoximes in 2*N*-solution have been determined and the effects of varying the concentrations of the reactants and of adding a common ion have been investigated, the results being summarised in Tables I and II.

Difficulties in technique make it impossible to claim a high standard of accuracy for the results, but repetitions have given sufficiently concordant values to justify the conclusion that they are approximately correct.

TABLE I.

(Sodium oximate, 2*N*.)

Oxime.	Ratio of *N*- : *O*-ether.	$10^{11} \times K_a$ of oxime.
α-3 : 4-Methylenedioxybenzaldoxime	1 : 1·86	1·4
α-*o*-Methoxybenzaldoxime	1·98	1·3
α-*p*-Methoxybenzaldoxime	2·16	1·2
α-Benzaldoxime	2·43	2·1
α-*m*-Methoxybenzaldoxime	2·60	2·6
α-*o*-Nitrobenzaldoxime	2·84	8·7
α-*m*-Nitrobenzaldoxime	3·62	7·0
α-2 : 4-Dinitrobenzaldoxime	12·0 *	37·0

* Only very approximate, as the amount of *N*-ether obtained was too small to be determined accurately.

TABLE II.

Oxime.	Ratio of *N*- : *O*-ether. 2*N*-Sodium oximate.	0·5*N*-Sodium oximate.	2*N*-Sodium oximate +2*N*-NaOH.	2*N*-Sodium oximate +4*N*-NaCl.
α-Benzaldoxime	1 : 2·43	—	—	1 : 2·00
α-*m*-Nitrobenzaldoxime	3·62	1 : 3·88	—	—
α-*p*-Methoxybenzaldoxime	2·16	2·59	1 : 2·65	1·86
α-3 : 4-Methylenedioxybenzaldoxime	1·86	2·55	2·61	—

Owing to the insolubility of the sodium salt of α-*p*-nitrobenzaldoxime, the methylation could be carried out only in 0·5*N*-solution and the ratio *N*- : *O*-ether was then 1 : 3·88; similar difficulties were experienced with other oximes in the presence of sodium chloride, etc.

The results are in harmony with the view that the *N*-ether is produced by the interaction of methyl sulphate with the undissociated sodium salt of the oxime, and the *O*-ether by an ionic reaction. For example, increasing the ionisation by dilution or by the addition of sodium hydroxide increases the amount of *O*-ether formed, whilst the addition of a common ion, thereby increasing the concentration of the sodium salt, results in more *N*-ether being produced (Table II). In addition, Table I indicates that the proportion of *N*-ether formed varies inversely as the magnitude of the dissociation constant. With *o*-methoxy-, *o*-nitro-, and 3 : 4-methylenedioxy-benzaldoximes, the amount of *N*-ether formed is greater than it should be, and in these cases there is apparently some other influence at work, possibly a steric one; it is noteworthy that ortho-substituted aldoximes are often anomalous in their behaviour.

It has already been shown that the β-aldoximes on methylation yield much more *N*- than *O*-ether (Brady, Dunn, and Goldstein, *loc. cit.*); for example, the ratios of *N*- to *O*-ether obtained from β-*p*-methoxy-, β-3 : 4-methylenedioxy-, and β-*m*-nitro-benzaldoximes were 1 : 0·11, 1 : 0·08, and 1 : 0·61, respectively; a similar explanation will account for this behaviour, since the β-aldoximes are much weaker acids than the corresponding α-compounds (Brady and Goldstein, this vol., p. 1923). The interaction of an α-aldoxime with methyl iodide or methyl sulphate to give exclusively the *N*-ether (Brady, Dunn, and Goldstein, *loc. cit.*) must also be represented as a molecular reaction, the hydriodide or methosulphate being the first product formed, R·CH:N·OH + MeI ⟶ R·CH:N(OH)MeI.

On this view, there are two simultaneous reactions proceeding

during the methylation of the sodium salts of the oximes: an ionic one giving the *O*-ether, and a molecular one the *N*-ether. With the high concentrations employed, it must also be assumed that the *O*-ether is produced in part by a molecular reaction by simple metathesis between the sodium salt of the oxime and methyl sulphate, on the analogy of the alkylation of the alcohols. By the application of Wegscheider's test it can be shown that the above reactions are all of the same order: Table III shows that the percentage of *N*-ether formed in the methylations at different stages is independent of the time.

TABLE III.

Oxime.	Wt. taken.	Wt. unacted upon.	% *N*-ether.
α-*m*-Nitrobenzaldoxime	5·00 g.	1·58 g.	20·2
,, ,, ...	5·00	0·82	20·8
α-*p*-Methoxybenzaldoxime	4·50	1·51	27·2
,, ,, ...	4·50	0·84	28·5
α-3 : 4-Methylenedioxybenzaldoxime	5·00	1·21	27·2
,, ,, ,,	5·00	0·88	27·5

The first two oximes were methylated in 0·5*N*-solution and the last in 2*N*-solution in the presence of excess of sodium hydroxide.

The amount of *N*-ether produced by methylating the sodium salts of two α-aldoximes with methyl iodide in alcoholic solution has also been determined, and it has been found that the proportion of *N*- to *O*-ether is approximately the same in 0·1*N*-alcoholic solution as in 2*N*-aqueous solution (compare Luxmoore, J., 1896, **69**, 186).

It must be pointed out that our interpretation of our results assumes that in 2*N*-solution there is a considerable amount of undissociated sodium oximate; if, however, the salts are completely dissociated at this concentration in accordance with recent theories of strong electrolytes, another explanation must be sought.

In connexion with this work, mention must be made of the investigations of Claisen (*Z. angew. Chem.*, 1923, **36**, 478; *Annalen*, 1925, **442**, 210) on the *C*-alkylation of phenols. He has shown, for example, that whilst, in dissociating solvents, sodium phenoxide and allyl bromide give more than 90% of allyl phenyl ether, in non-dissociating media as much as 70% of *o*-allylphenol is produced. It appears, therefore, that the views developed in this paper are of wide application; it has already been found that they can be applied to the methylation of the hydroxybenztriazoles (Brady and Day, J., 1923, **123**, 2258, and unpublished work) and we propose to extend it in other directions.

EXPERIMENTAL.

Determination of β-Methylhydroxylamine.—The β-methylhydroxylamine hydrochloride was prepared by the reduction of nitromethane with zinc dust in neutral solution (Beckmann, *Annalen*, 1909, **365**, 204); it is best purified by two or three crystallisations from a mixture of boiling absolute alcohol and ethyl acetate, washing the crystals with dry ether, and drying over potassium hydroxide in a vacuum, being then obtained in colourless, odourless crystals, m. p. 88—89°. The method of purification described in the literature—precipitation of a solution in absolute alcohol with ether—is unsatisfactory.

According to Kirpal (*Ber.*, 1892, **25**, 1715), β-methylhydroxylamine can be determined by weighing the cuprous oxide it precipitates from boiling Fehling's solution according to the equation

$$3CH_3{\cdot}NH{\cdot}OH + 6CuO = 3Cu_2O + CH_3{\cdot}NH_2 + 2NH_3 + 2CO_2 + 2H_2O.$$

We cannot confirm this statement, since, when β-methylhydroxylamine was boiled with Fehling's solution, very variable results were obtained, 1 mol. requiring, *e.g.*, $\frac{7}{8}$, $2\frac{3}{4}$, $3\frac{1}{4}$, and $1\frac{3}{4}$ atoms of oxygen.

An alternative possibility was the reduction of iodine in potassium iodide by β-methylhydroxylamine hydrochloride in the presence of sodium bicarbonate, and after some trouble satisfactory conditions have been devised for obtaining concordant results. A roughly *N*/10- to *N*/20-solution of β-methylhydroxylamine hydrochloride was run into a mixture of 25 c.c. of *N*/30-iodine in potassium iodide, 75 c.c. of water, and 75 c.c. of a saturated solution of sodium bicarbonate. With the burette used (time of flow for 50 c.c. = 35 secs.), about four-fifths of the necessary amount of the β-methylhydroxylamine solution was run in all at once without shaking, and the rest more slowly, the end-point being determined by starch indicator; the temperature of the iodine solution was kept at 10—15°. Under these conditions concordant titration values could be obtained and the reaction appears to be stoicheiometrical, 1 mol. of β-methylhydroxylamine requiring 2 atoms of iodine. The method was checked against β-methylhydroxylamine hydrochloride and against two *N*-ethers. For example, 0·5083 g. of β-methylhydroxylamine hydrochloride was dissolved in water and diluted to 250 c.c.; successive portions of 25 c.c. of 0·03256*N*-iodine, diluted as before, required 16·9, 17·0, and 16·8 c.c. (mean 16·9) of the β-methylhydroxylamine solution. If the reaction is stoicheiometrical, this indicates 98·9% of β-methylhydroxylamine hydrochloride in the sample used. Again, 0·9725 g. of *N*-methyl-*m*-nitrobenzaldoxime was boiled under reflux with 10 c.c. of concentrated hydrochloric acid and 5 c.c. of water for 20 minutes, and the

m-nitrobenzaldehyde formed by hydrolysis was removed by extraction with chloroform. The aqueous residue was neutralised with the calculated amount of potassium bicarbonate, made up to 250 c.c., and the β-methylhydroxylamine determined as above. Successive amounts of 25 c.c. of the iodine solution required 19·3, 19·4, 19·2, 19·5, and 19·2 c.c. of the above solution (mean 19·3), giving 97·5% of *N*-ether in the sample taken. Finally, 0·9368 g. of *N*-methyl-3 : 4-methylenedioxybenzaldoxime was treated as above, 25 c.c. of the iodine solution requiring 19·6, 19·8, and 19·8 c.c. (mean 19·7 c.c.) of the β-methylhydroxylamine solution, indicating 98·6% of *N*-ether in the sample taken.

We have not yet been able to identify with certainty the products of the oxidation of β-methylhydroxylamine under these conditions, but it seems probable that formaldoxime is the primary product ($CH_3 \cdot NH \cdot OH + O = CH_2 \cdot N \cdot OH + H_2O$). In any case, Kirpal's equation cannot apply, since no methylamine could be detected in the reaction mixture by Valton's method (J., 1925, **127**, 40), and boiling with alkali for 2 hours gave only 10% of the nitrogen as ammonia. The reaction is being further investigated.

The Quantitative Methylation of the Aldoximes.—(*a*) *In* 2N-*solution.* The general method was as follows : The oxime (0·03 g.-mol.) was dissolved in 18 c.c. of 2*N*-sodium hydroxide (0·036 g.-mol.) and 3 c.c. of methyl sulphate (0·032 g.-mol.), previously washed and dried over anhydrous sodium sulphate, were added. The mixture was cooled under the tap and shaken frequently for 10—20 minutes. The combined ethers formed were extracted with several portions of chloroform, and the extracted mixed ethers, after evaporation of the solvent, were boiled with 10 c.c. of concentrated hydrochloric acid and 5 c.c. of water under reflux for ½—1½ hours; aldehyde and *O*-ether were removed by extraction with chloroform and the β-methylhydroxylamine in the aqueous solution was determined as above. Meanwhile, the unchanged oxime left in the aqueous portion of the methylation mixture after removal of the ethers was determined by adding a saturated solution of ammonium chloride and extracting with chloroform. The solvent was removed on the water-bath, and the oxime dried in the steam-oven and weighed. The results are accurate to within about 5%. The direct determination of the *O*-ether proved to be impracticable owing to its volatility.

The total yield of ethers (*T*) was calculated from the amount of oxime methylated, as determined from the difference between the quantities employed and recovered (*W*, *w*), and the yield of *N*-ether (*N*) from the β-methylhydroxylamine, the ratio of *N*- to *O*-ether being given by $N : (T—N)$. The results are given in Table IV.

TABLE IV.

Oxime.	*W.*	*w.*	*N.*	*T.*	$100N/T$.	$N:(T-N)$.
α-Benzaldoxime (1)	3·60 g.	0·30 g.	1·09 g.	3·68 g.	29·6	1 : 2·36
,, ,, (2)	3·60	0·16	1·10	3·84	28·6	2·49
α-*o*-Nitrobenzaldoxime (1) ...	5·00	0·38	1·30	5·01	25·9	2·85
,, ,, (2) ...	5·00	0·42	1·30	4·97	26·2	2·82
α-*m*-Nitro- ,, (1) ...	5·00	0·34	1·11	5·05	22·0	3·55
,, ,, (2) ...	5·00	0·33	1·08	5·06	21·3	3·69
α-2 : 4-Dinitro- ,, ...	3·61*	2·50	0·09	1·18	7·6	12·1
α-*o*-Methoxy- ,, ...	3·00†	0·16	1·04	3·10	33·5	1·98
α-*m*-Methoxy- ,, ...	4·50	0·38	1·25	4·50	27·8	2·60
α-*p*-Methoxy- ,, (1) ...	4·50	0·04	1·52	4·87	31·2	2·20
,, ,, (2) ...	4·50	0·11	1·54	4·80	32·1	2·12
α-3 : 4-Methylenedioxybenzaldoxime (1)	5·00	0·35	1·77	5·05	35·0	1·85
α-3 : 4-Methylenedioxybenzaldoxime (2)	5·00	0·33	1·76	5·07	34·7	1·88

* With 2 : 4-dinitrobenzaldoxime, 10·25 c.c. of 2*N*-sodium hydroxide and 1·7 c.c. of methyl sulphate were used; owing to the very low concentration of β-methylhydroxylamine in the solution for titration, the value for *N* is inaccurate, but the experiment goes to show that a low proportion of *N*-ether is formed on methylation.

† Using 12 c.c. of 2*N*-sodium hydroxide and 2 c.c. of methyl sulphate.

(*b*) *In* 0·5N-*solution.* The oximes (0·03 g.-mol) dissolved in 72 c.c. of 0·5*N*-sodium hydroxide (0·036 g.-mol.) were methylated with 3 c.c. of methyl sulphate under similar conditions and the product was treated as before; the results are given in Table V.

TABLE V.

Oxime.	*W.*	*w.*	*N.*	*T.*	$100N/T$.	$N:(T-N)$.
α-*m*-Nitrobenzaldoxime (1) ...	5·00 g.	0·82 g.	0·94 g.	4·53 g.	20·8	1 : 3·82
,, ,, (2) ...	5·00	1·58	0·75	3·71	20·2	3·95
α-*p*-Nitro- ,, (1) ...	5·00	1·75	0·74	3·52	21·0	3·76
,, ,, (2) ...	5·00	1·42	0·78	3·89	20·1	3·99
α-*p*-Methoxy- ,, (1) ...	4·50	1·51	0·89	3·27	27·2	2·67
,, ,, (2) ...	4·50	0·84	1·14	4·00	28·5	2·51
α-3 : 4-Methylenedioxybenzaldoxime (1)	5·00	0·77	1·27	4·59	27·7	2·61
α-3 : 4-Methylenedioxybenzaldoxime (2)	5·00	0·84	1·29	4·51	28·6	2·50

(*c*) *In excess of sodium hydroxide.* The amounts of material taken were: oxime, 0·030 g.-mol.; 4*N*-sodium hydroxide, 18 c.c. (0·072 g.-mol.); and methyl sulphate, 3 c.c. (0·032 g.-mol.).

(*d*) *In the presence of sodium chloride.* The amounts of material taken were: oxime, 0·030 g.-mol.; 2*N*-sodium hydroxide, 18 c.c. (0·036 g.-mol); sodium chloride, 4·27 g. (0·073 g.-mol.); and methyl sulphate, 3 c.c. (0·032 g.-mol.).

The results of both (*c*) and (*d*) are given in Table VI.

TABLE VI.

Oxime.	*W.*	*w.*	*N.*	*T.*	$100N/T$.	$N:(T-N)$.
			(*c*) In excess of sodium hydroxide.			
α-*p*-Methoxybenzaldoxime (1)	4·50 g.	0·73 g.	1·12 g.	4·12 g.	27·2	1 : 2·68
,, ,, (2)	4·50	0·68	1·15	4·17	27·6	2·63
α-3 : 4-Methylenedioxybenzaldoxime (1)	5·0	1·21	1·12	4·11	27·3	2·67
α-3 : 4-Methylenedioxybenzaldoxime (2)	5·0	0·88	1·25	4·47	28·0	2·58
			(*d*) In presence of sodium chloride.			
α-Benzaldoxime (1)	3·60	0·18	1·30	3·82	34·0	1·94
,, (2)	3·60	0·17	1·25	3·83	32·6	2·06
α-*p*-Methoxybenzaldoxime (1)	4·50	0·04	1·73	4·87	35·7	1·82
,, ,, (2)	4·50	0·06	1·68	4·85	34·6	1·89

The means of the values given in the foregoing tables were used in the theoretical part.

Methylations in the presence of excess of sodium hydroxide or of sodium chloride could not be carried out with a larger number of oximes owing to the precipitation of the sodium salt.

(*e*) *In alcoholic solution.* (1) α-*m*-Nitrobenzaldoxime. Sodium (0·74 g.; 0·032 g.-mol.) was dissolved in 301 c.c. of absolute alcohol and pure α-*m*-nitrobenzaldoxime (5·00 g.; 0·030 g.-mol.) added, giving an *N*/10-solution; methylation was effected by pure redistilled methyl iodide (4·54 g.; 0·032 g.-mol.); after being kept for 18 days the solution reacted neutral. Concentrated hydrochloric acid (10 c.c.) was added and the solution distilled in steam for 3 hours to remove alcohol, aldehyde, and *O*-ether, and the β-methylhydroxylamine hydrochloride remaining in the flask was determined. A preliminary experiment had shown that α-*m*-nitrobenzaldoxime was completely methylated by the action of a slight excess of methyl iodide and sodium in alcohol over a period of 3 days. Oxime taken = 5·00 g.; *N*-ether found = 0·92 g.; total amount of ethers formed = 5·42 g.; percentage of *N*-ether = 17·0; ratio of *N*- to *O*-ether = 1 : 4·89.

(2) α-3 : 4-Methylenedioxybenzaldoxime. The following quantities were used: oxime, 4·87 g. (0·029 g.-mol.); methyl iodide, 4·34 g. (0·030 g.-mol.); sodium, 0·71 g. (0·031 g.-mol.); and absolute alcohol, 295 c.c.; after 17 days, the product was treated as before: *N*-ether found = 1·90 g.; total ethers formed = 5·28 g.; percentage of *N*-ether = 36·0; ratio of *N*- to *O*-ether = 1 : 1·78.

Summary.

(1) The relative amounts of *O*- and *N*-ethers formed under various experimental conditions in the methylation of the aldoximes have been determined.

(2) The results are in agreement with the assumption that the *O*-ether is produced essentially by an ionic reaction between the oxime ion and the alkyl compound, and that the *N*-ether is produced by addition of the alkyl compound to the undissociated sodium oximate.

In conclusion, one of us (R. F. G.) wishes to thank the Department of Scientific and Industrial Research for a maintenance grant which enabled him to take part in this work.

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CCCXX.—*The Isomerism of the Oximes. Part XXVIII. The Beckmann Rearrangement of the* N-*Methyl Ethers of Aldoximes.*

By OSCAR L. BRADY and FREDERICK P. DUNN.

BECKMANN (*Annalen*, 1909, **365**, 201) showed that *N*-methylbenzaldoxime on treatment with phosphorus pentachloride underwent rearrangement to benzomethylamide, PhCH:NMe:O → PhCO·NHMe, but this isolated observation in a paper not dealing specifically with the Beckmann rearrangement seems to have escaped notice. We have now found that this is a general reaction with *N*-methyl ethers of aldoximes and occurs with great ease on heating them with acetic anhydride to a temperature just below the b. p. of the reagent; indeed, with *N*-methylbenzaldoxime the reaction is extremely violent; the method is clean and no tarry by-products are formed. If the reaction mixture is cooled at once, in six out of the seven compounds investigated the amide itself is obtained and not the acetylated substance, and in the cases of *N*-methyl-*m*- and -*p*-nitrobenzaldoximes, it crystallises from the acetic anhydride on cooling. This is noteworthy since the methylamides are readily acetylated on boiling with acetic anhydride, and the reaction is of special interest since in these two cases the ultimate product of the Beckmann rearrangement is isolated without the final hydrolytic treatment which is required when phosphorus pentachloride is employed.

It is at once obvious that the numerous theories * of the mechanism of the Beckmann rearrangement involving the form-

* The relevant papers are too numerous to quote. The various theories are fairly fully discussed in Johnson and Hahn's translation of Henrich's "Theories of Organic Chemistry," 1922, pp. 131—134, and Chapter XIX.

ation of an intermediate compound containing univalent nitrogen are here impossible; indeed, even Stieglitz has abandoned the notion on finding that β-triphenylmethyl-β-methylhydroxylamine suffers rearrangement to phenylmethylaminodiphenylcarbinol,

$$CPh_3{\cdot}NMe(OH) \longrightarrow CPh_2(OH){\cdot}NMePh$$

(Stieglitz and Leech, *J. Amer. Chem. Soc.*, 1914, **36**, 272). The fact that dehydrating agents are employed to bring about the Beckmann rearrangement has in the past strongly favoured the theory that the change is preceded by the elimination of water from a salt of the oxime, but Lachmann (*J. Amer. Chem. Soc.*, 1924, **46**, 1477; 1925, **47**, 260) has discredited this by bringing about the reaction in the presence of water. The behaviour of the *N*-methylbenzaldoximes supports the work of Lachmann, as it is difficult in this instance to devise a mechanism by which water can be eliminated. Lachmann has also shown that it is the hydrochloride and not the oxime which undergoes rearrangement when phosphorus pentachloride is used (see also Henrich, *Ber.*, 1911, **44**, 1533) and it is noteworthy that the *O*-methyl ethers of the aldoximes, which are devoid of basic properties, are not rearranged. The *N*-ethers may be regarded as containing "quinquevalent" nitrogen in themselves (compare Sugden, J., 1925, **127**, 1532), but in any case they readily form salts and it is becoming increasingly evident that the fundamental basis of isomeric change in the oximes is always dependent on the change in valency of the nitrogen atom.

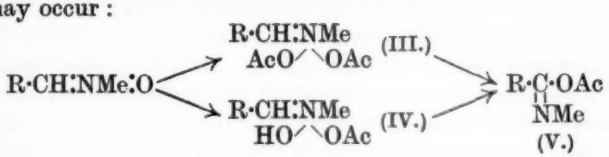
We are of opinion that any explanation of the Beckmann rearrangement must have regard to the following considerations: (1) the rearranging compound must be a salt or a salt-like substance; (2) the elimination of water or the formation of a univalent nitrogen compound must not be essential postulates; and (3) the rupture of the carbon–nitrogen double bond must not be involved before the interchange of radicals takes place.

That condition (3) must be satisfied seems essential, since, in a mechanism such as was at one time suggested by Stieglitz (*Amer. Chem. J.*, 1896, **18**, 754; 1911, **46**, 327) and supported by Schroeter (*Ber.*, 1909, **42**, 2337, 3386; 1911, **44**, 1201), there is no adequate reason why the stereoisomeric ketoximes should give different amides, because (I) and (II) as prepared from either oxime must be racemic mixtures of two enantiomorphs and give the same products on changing.

$$\begin{matrix} R \\ R' \end{matrix}\!\!>\!C{:}NOH \longrightarrow \underset{\text{(I.)}}{\begin{matrix} R \\ R' \end{matrix}\!\!>\!C\!<\!\begin{matrix} Cl \\ NOH \\ | \\ H \end{matrix}} \longrightarrow \underset{\text{(II.)}}{\begin{matrix} R \\ R' \end{matrix}\!\!>\!C\!<\!\begin{matrix} Cl \\ N\cdots \end{matrix}} \longrightarrow$$

$$RCCl{:}NR' + R'CCl{:}NR \longrightarrow R{\cdot}CO{\cdot}NHR' + R'{\cdot}CO{\cdot}NHR.$$

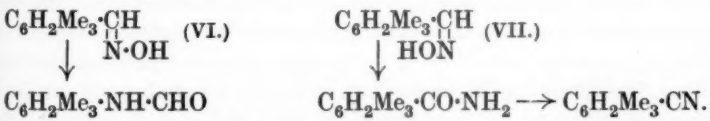
That elimination of water is not essential seems obvious if one considers the possible intermediate compounds in the rearrangement of the *N*-ethers; addition of acetic anhydride (III) or acetic acid (IV) may occur:



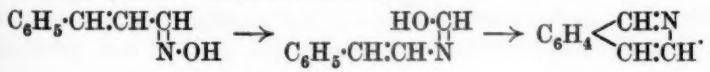
The elimination of acetic acid or water can take place only if the hydrogen attached to the carbon atom is involved, otherwise the *N*-ether would be re-formed; rearrangement would then involve the migration of the OAc group and it seems inconceivable, if compound (V) was formed, that the unacetylated methylamide R·CO·NHMe would crystallise from the excess of acetic anhydride.

The rearrangement of the *N*-ethers supplies the first indication of the configuration of these compounds. Unless the hydrogen atom is so mobile in comparison with the phenyl group that it migrates preferentially, we must assume that there is a definite orientation of the oxygen atom with respect to the groups attached to carbon. Accepting Meisenheimer's view that the Beckmann rearrangement takes place in the *trans*-direction, the change may be represented as

that is, the *N*-ethers have constitutions analogous to the β-oximes. Little work has been done on the Beckmann rearrangement of the aldoximes, but Comstock (*Amer. Chem. J.*, 1897, **19**, 485) has shown that the β-oximes give amides on treatment with cuprous chloride, and Hantzsch and Lucas (*Ber.*, 1895, **28**, 744) found that with phosphorus pentachloride α-mesitylaldoxime (VI) gave formmesidide, and the β-oxime (VII) trimethylbenzonitrile, probably through the amide:



Moreover, the formation of *iso*quinoline, and not quinoline, by the action of phosphorus pentoxide on cinnamaldoxime (Bamberger and Goldschmidt, *Ber.*, 1894, **27**, 1954) may, perhaps, be regarded as the result of a Beckmann rearrangement:



These two reactions indicate that one cannot assume that the hydrogen atom in the *N*-ether will migrate exclusively.

In the light of this work, the symmetrical formula for the *N*-ethers suggested by one of us (J., 1914, **105**, 2104) cannot be maintained, neither can the argument, there put forward, that a stable α-*N*-ether may be formed during the methylation. It may also be pointed out that the suggested constitution of the sodium salt of the oxime used in connexion with the above argument is not in accord with modern views on the structure of the nitrogen atom. We have, therefore, no explanation of the fact that, whereas some unsymmetrical ketoximes give two *N*-ethers, aldoximes give but one (compare Brady, Dunn, and Goldstein, this vol., p. 2388).

Finally, we have been able to obtain a small yield of the methylamide by heating the hydrochloride of *N*-methyl-*m*-nitrobenzaldoxime; in other cases investigated, so much tar was formed that isolation of crystalline compounds was impossible.

Experimental.

The *N*-methyl ether was dissolved or suspended in five times its weight of pure, cold acetic anhydride and the mixture warmed cautiously on the sand-bath; in most cases, just before the b. p. of the anhydride was reached, there was a vigorous reaction and the solution boiled—in the case of *N*-methylbenzaldoxime, the reaction occurs at a lower temperature with almost explosive violence; the mixture was then cooled rapidly.

With *N*-methyl-*p*-nitrobenzaldoxime, the large quantity of solid which separated was collected, pressed on a porous tile, and crystallised from alcohol, giving *p*-nitrobenzomethylamide, m. p. 217°. With *N*-methyl-*o*-nitrobenzaldoxime, the excess of anhydride was decomposed with 2*N*-sodium carbonate and the precipitated *o*-nitrobenzomethylamide was collected, dried on a porous tile, and crystallised from benzene; m. p. 107°. With *N*-methyl-*m*-nitrobenzaldoxime, when the reaction mixture was cooled in ice, nearly pure *m*-nitrobenzomethylamide separated; a further quantity was obtained by treating the mother-liquor with sodium carbonate solution; one crystallisation from benzene gave the pure compound. With *N*-methylbenzaldoxime, after being treated with sodium carbonate, the mixture was extracted with chloroform; on removal of the solvent, the residual oil solidified on scratching, and after pressing on a porous tile and crystallising from benzene–light petroleum gave benzomethylamide (m. p. 78°). With 3 : 4-methylenedioxybenzaldoxime, the solid obtained after sodium carbonate treatment was crystallised from benzene–light petroleum and 3 : 4-methylenedioxybenzomethylamide (m. p. 136°) was obtained.

N-Methylcinnamaldoxime, after sodium carbonate treatment, gave an oil which solidified on keeping. The solid was collected, pressed on a porous tile and a small amount reserved; the rest was dissolved in benzene, light petroleum was added cautiously, and the solution seeded with a fragment of the reserved material, whereupon cinnamomethylamide (m. p. 111°) crystallised. With *N*-methyl-*o*-methoxybenzaldoxime, after sodium carbonate treatment and extraction with chloroform, an uncrystallisable oil was obtained; this was boiled under reflux with concentrated alcoholic potassium hydroxide for 8 hours, methylamine being evolved and identified by Valton's method (J., 1925, **127**, 40). The solution was diluted and extracted with chloroform to remove unchanged material, and the aqueous layer acidified with hydrochloric acid and again extracted with chloroform; on evaporation of the solvent and crystallisation of the residue from dilute alcohol, *o*-methoxybenzoic acid (m. p. 101°) was obtained and identified by comparison.

In every case except the last, the methylamide was identified by the method of mixed m. p.'s with a sample prepared in another way.

Some of these compounds have not been previously described. *o*-Nitrobenzoyl chloride (5 g.) was added to methylamine (6 c.c. of 30% solution diluted with 25 c.c. of water) and the mixture shaken for some minutes; the solid formed, after being collected, washed, dried, and crystallised from benzene to which a little light petroleum had been added, gave *o-nitrobenzomethylamide* in short, colourless, prismatic needles, m. p. 107° (Found: N, 15·8. $C_8H_8O_3N_2$ requires N, 15·6%). Ethyl 3 : 4-methylenedioxybenzoate was added to excess of 33% methylamine and enough methyl alcohol added to give a clear solution. After 5 days at room temperature, water was added and the solid collected, dried on a porous tile, and crystallised from benzene–light petroleum; 3 : 4-*methylenedioxybenzomethylamide* was thus obtained in slightly brown needles, m. p. 136° (Found: N, 8·0. $C_9H_9O_3N$ requires N, 7·8%). Cinnamomethylamide may be easily prepared in a similar way from ethyl cinnamate, by seeding the mixture after dilution with a trace of the methylamide and recrystallising the product from benzene–light petroleum with seeding.

In carrying out the Beckmann change with the *N*-ethers, it is important not to boil with acetic anhydride for any length of time, otherwise the methylamide is acetylated; for example, *p*-nitrobenzomethylamide was boiled with excess of acetic anhydride for 2 hours under reflux; after cooling and treatment with 2*N*-sodium carbonate, the solid obtained was crystallised twice from alcohol and found to be *aceto*-p-*nitrobenzomethylamide*, colourless prisms, m. p. 125° (Found: N, 12·8. $C_{10}H_{10}O_4N_2$ requires N, 12·6%). On heating

on the water-bath with concentrated hydrochloric acid, the compound dissolved and *p*-nitrobenzomethylamide slowly crystallised from the solution; warming with concentrated sulphuric acid and alcohol gave ethyl acetate. The same compound was obtained from *N*-methyl-*p*-nitrobenzaldoxime by boiling with acetic anhydride for 1 hour.

In spite of all precautions, such as rapid cooling immediately the violent reaction occurred, *p*-methoxybenzomethylamide could not be obtained from *N*-methyl-*p*-methoxybenzaldoxime, the product being invariably the acetylated compound. This was synthesised for comparison by boiling anisic acid (4 g.) under reflux with thionyl chloride (25 c.c.) for 1 hour, removing the excess of thionyl chloride on the water-bath under reduced pressure, and pouring the remaining anisoyl chloride into a mixture of methylamine (6 c.c. of 33% solution), water (18 c.c.), and 2*N*-sodium hydroxide (25 c.c.), shaking, and keeping for 30 minutes. The granular precipitate was collected, washed, and crystallised from benzene and then from hot water, giving p-*methoxybenzomethylamide* in brilliant, colourless needles, m. p. 116° (Found: N, 8·8. $C_9H_{11}O_2N$ requires N, 8·5%). This compound was boiled with acetic anhydride under reflux for 1 hour and the solution cooled and poured into excess of ice-cold 2*N*-sodium carbonate; after shaking until free from anhydride, the precipitate was crystallised from dilute alcohol and gave *aceto*-p-*methoxybenzomethylamide* as white plates, m. p. 50° (Found: N, 6·9. $C_{11}H_{13}O_3N$ requires N, 6·8%). Hydrolysis by boiling with concentrated hydrochloric acid for 30 minutes gave anisic acid.

The hydrochloride of *N*-methyl-*m*-nitrobenzaldoxime, on being heated at 100° for 2½ hours in a tube to which a calcium chloride guard-tube was attached, underwent no appreciable change; on being heated, however, at 168—170° in an oil-bath for 20 minutes, the hydrochloride slowly melted and then decomposed with evolution of hydrogen chloride; when this had ceased, the melt was cooled, the brown mass ground up and extracted with boiling acetone, the solvent removed and the tarry residue extracted with a little boiling benzene; on cooling the solution, *m*-nitrobenzomethylamide separated. When *O*-methyl-*m*-nitrobenzaldoxime was boiled for 2 hours with acetic anhydride and the solution treated with excess of sodium carbonate solution, the ether was recovered unchanged.

In conclusion, we wish to express our thanks to Dr. R. F. Goldstein for help with the experimental work.

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CCCXXI.—*The Reaction between Picryl Chloride and Pyridine in Alcoholic Solution.*

By Francis William Hodges.

Picryl chloride reacts very slowly with anhydrous alcohol even at 70°, but somewhat more rapidly with alcohol which has not been specially dried. It was anticipated that pyridine, by combining with the two acids formed by hydrolysis, would accelerate the reaction, and conductivity measurements with *M*/40- and *M*/80-solutions of pyridine and picryl chloride at 18·3° indicated a fairly rapid formation of ionised products. These alcoholic solutions slowly deposited lustrous, brown crystals, m. p. *ca.* 220°, and concentration of the remaining solution yielded pyridine picrate. The crystals were subsequently found to be picrylpyridinium picrate, $C_5H_5N<\begin{matrix}C_6H_2(NO_2)_3\\O\cdot C_6H_2(NO_2)_3\end{matrix}$. Analogous compounds have been prepared by Barnett and Cook (J., 1922, **121**, 792).

Since Wedekind (*Annalen*, 1902, **313**, 257) had isolated an additive compound of pyridine and picryl chloride, containing one molecule of each, from benzene solutions, it was thought that this compound might constitute an intermediate stage in the reaction under discussion. Wedekind's compound, m. p. 138°, was prepared, and its alcoholic solution slowly deposited crystals which were identical with those described above, although Wedekind had stated that the products of hydrolysis of his compound were pyridine picrate and hydrochloric acid.

On the assumption that this additive compound was the first intermediate product, the whole reaction was formulated as follows:

$$C_5H_5N + C_6H_2Cl(NO_2)_3 = C_5H_5N,C_6H_2Cl(NO_2)_3 \text{ (slow)} \quad . \quad . \quad (1)$$

$$C_5H_5N,C_6H_2Cl(NO_2)_3 + H_2O = C_5H_5N,C_6H_2(NO_2)_3\cdot OH + HCl \text{ (rapid)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$C_5H_5N + HCl = C_5H_5N,HCl \text{ (instantaneous)} \quad . \quad . \quad . \quad . \quad . \quad (3)$$

these being accompanied by slow side reactions giving picrylpyridinium picrate and ethyl picrate (from the alcohol). The measurable reaction should therefore be bimolecular, and unimolecular with regard to each reactant.

The net effect of the above equations is

$$2C_5H_5N + C_6H_2Cl(NO_2)_3 + H_2O = C_5H_5N,HCl + C_5H_5N,C_6H_2(NO_2)_3\cdot OH.$$

Representing the initial concentrations of picryl chloride and

pyridine as a and b, respectively, and the amount of pyridine picrate produced after time t as x, one has

$$dx/dt = k(b - 2x)(a - x) \quad . \quad . \quad . \quad . \quad (4)$$

The results obtained at 23·2° gave fair constancy for the velocity coefficients based on this assumption.

At higher temperatures, however, it is clear that this equation does not represent the reaction; in fact, at two different temperatures the concentration–time curves actually intersect. The initial velocity is greater for the higher temperature, but the velocity decreases more rapidly with time, so that, for a given degree of reaction above a certain value, the velocity is lower at the higher temperature. This result suggests an equilibrium reaction in which the equilibrium point is displaced with rising temperature in a direction which diminishes the concentration of one of the reactants in the principal reaction.

The assumption that pyridine in reaction (1) was replaced by pyridinium hydroxide, formed in relatively very small concentration by the mass-action equilibrium between pyridine and water, led to an equation similar in form to (4), but which demanded that the velocity should be directly proportional to the water concentration, and this was not in agreement with the experimental results (see Tables A, III and IV). A clue was sought in the colour changes which occur during the course of the reaction; the slow development of colour with the progress of the reaction, the fact that it was less pronounced at the higher temperatures, and its resemblance to that produced by Wedekind's additive compound in alcoholic solution, all pointed to the intermediate formation of this compound in equilibrium with pyridine and picryl chloride. Moreover, such a development of colour has been attributed to the formation of additive compounds of this nature by various workers (Burton and Kenner, J., 1921, ,119 1047; Kenner and Parkin, *ibid.*, 1920, **117**, 852; Sudborough and Picton, *ibid.*, 1906, **89**, 583; Hibbert and Sudborough, *ibid.*, 1903, **83**, 1336).

When Wedekind's compound was dissolved in cold alcohol, the concentration of the chloride ion *decreased* (Table B), whereas the addition of an alcoholic solution of picryl chloride caused an *increase*. These results point clearly to the chlorine in the additive compound being ionic, and to the slow dissociation of this substance into its constituents until an equilibrium point is reached, this equilibrium being displaced in the direction of less dissociation by the addition of picryl chloride.

The formation of pyridine picrate might take place (*a*) by the direct hydrolysis of the additive compound, or (*b*) by a side

reaction between picryl chloride and water, pyridine acting as a catalyst.

The following facts supported the latter view:

1. The yield of ethyl picrate is considerably increased in the presence of pyridine and it seems reasonable to suppose that the corresponding reaction between picryl chloride and water would be similarly catalysed.

2. When the reaction is carried out in the presence of excess of water, the predominating reaction is that giving pyridine picrate.

3. When the reaction was followed by the conductivity method, a perfectly smooth curve was obtained, whereas, with two consecutive reactions, of which the second results in the formation of hydrogen ions, there should be an induction period.

The course of the reaction is therefore assumed to be

$$C_5H_5N + C_6H_2Cl(NO_2)_3 \rightleftharpoons C_5H_5{:}NCl{\cdot}C_6H_2(NO_2)_3 \text{ (slow)} \quad . \quad . \quad (5)$$

$$C_5H_5N + C_6H_2Cl(NO_2)_3 + H_2O \longrightarrow C_5H_5{:}N(OH){\cdot}C_6H_2(NO_2)_3 + HCl \text{ (slow side reaction)} \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$C_5H_5{:}N(OH){\cdot}C_6H_2(NO_2)_3 + C_6H_2Cl(NO_2)_3 \longrightarrow C_5H_5N\begin{matrix}<\\ \\ \end{matrix}\begin{matrix}O{\cdot}C_6H_2(NO_2)_3\\ C_6H_2(NO_2)_3\end{matrix} + HCl \text{ (very slow)} \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$C_6H_2Cl(NO_2)_3 + C_2H_5{\cdot}OH \longrightarrow C_6H_2(NO_2)_3{\cdot}O{\cdot}C_2H_5 + HCl \text{ (slow)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

$$C_5H_5N + HCl \longrightarrow C_5H_5N,HCl \text{ (instantaneous)} \quad . \quad . \quad . \quad . \quad . \quad (9)$$

Reaction (5) appears to be the main reaction and leads to the equation

$$dx/dt = k_1(a - x)(b - x) - k_2x \quad . \quad . \quad . \quad (10)$$

which, on integration, gives

$$k_1nt = \log_e (m - n)(m + n - 2x)/(m + n)(m - n - 2x),$$

where $m = a + b + K$ and $n^2 = (a + b + K)^2 - 4ab$, K being the equilibrium constant.

Reactions (7) and (8) each result in the disappearance of one equivalent of picryl chloride and one equivalent of pyridine, with the corresponding formation of one equivalent of hydrochloric acid, the only effect on the equilibrium being due to reduced ionisation of the additive compound and a consequent slight displacement in the direction of greater dissociation. Reaction (6) involves the disappearance of one equivalent of picryl chloride and two equivalents of pyridine, this again resulting in greater dissociation.

The combined effect of these side reactions would be expected to cause a reduced value for k_1 as the reaction proceeds, and this was actually the case. The effect is more marked at the higher

concentrations, but is less marked in dried alcohol. It is seen from the tables that this hypothesis is fairly well substantiated by the results.

The addition of an increasing excess of water apparently causes reaction (6) to have greater influence and finally to predominate, no equilibrium point being obtainable (Tables A, III and IV). A similar effect is obtained with a large excess of pyridine. Evidence for this explanation was obtained when the reaction was carried out in bulk, and with a large excess of pyridine or of water. In both cases, a far higher yield of pyridine picrate was obtained.

EXPERIMENTAL.

A. *Preparation of Picrylpyridinium Picrate.*—Picryl chloride (6·19 g.) and pyridine (2 g.) were heated under reflux with 100 c.c. of absolute alcohol for 4 hours. On cooling, 4·4 g. of lustrous, brown crystals were deposited. This compound was insoluble in alcohol, glacial acetic acid, benzene, ether, or light petroleum, but soluble in acetone, pyridine, or glycerol, and moderately easily soluble in nitrobenzene. It dissolved in 50% aqueous alcohol, from which it separated in golden-yellow crystals, m. p. 226° (decomp.) (Found: C, 39·5; H, 2·3; N, 18·8; *M*, in acetone, 521; *M*, in nitrobenzene, 519. Calc.: C, 39·4; H, 1·8; N, 18·9%; *M*, 519). With potash, it gives pyridine on heating.

Further proof of the composition was obtained by grinding picrylpyridinium chloride and sodium picrate under acetone. The residue after evaporation was boiled with water and filtered. The brown residue, m. p. 223°, was identical with the compound already described.

B. *Isolation of Other Products of the Reaction.*—After the removal of picrylpyridinium picrate from the main reaction mixture, small quantities of pyridine picrate and ethyl picrate were obtained. A solution of 12·4 g. of picryl chloride and 4 g. of pyridine in 100 c.c. of absolute alcohol was boiled under reflux for 1 hour. The yield was about 1 g. of picrylpyridinium picrate, and, on concentration of the filtrate, 6 g. of the additive compound, which, on being boiled with excess of alcohol, gave picrylpyridinium picrate. Similar treatment with 50% aqueous alcohol gave chiefly pyridine picrate.

Repetition of the first experiment, excess of pyridine or equivalent quantities in 75% aqueous alcohol being used, gave pyridine picrate as the main product.

C. *Velocity Measurements.*—At the outset the following method was employed for investigating the rate of formation of the additive compound. Measured quantities of the reaction mixture were

transferred at intervals to a flask containing a known excess of nitric acid. Excess of a solution of potassium iodide and iodate in the proportions required by the equation $5KI + KIO_3 + 6HNO_3 = 6KNO_3 + 3H_2O + 3I_2$ was then added, and the liberated iodine was titrated with sodium thiosulphate. Although the method was not considered sufficiently accurate for velocity measurements, it served to show that there was a small gradual decrease in the amount of pyridine present, so that the first reaction, resulting in the formation of picrylpyridinium chloride, was comparatively slow.

Rheinlander (J., 1923, **123**, 3099), investigating the reactions between picryl halogen compounds and aniline hydrochloride, and other reactions of a similar nature, made use of the method described below. This was found to be more satisfactory and was employed throughout.

Measured quantities (10 c.c.) of the reaction mixture were transferred at intervals to a separator containing 20 c.c. of benzene, 10 c.c. of dilute nitric acid, and 20 c.c. of $N/80$-silver nitrate. Vigorous shaking resulted in the absorption of the coloured compounds by the benzene layer; the greater part of the silver chloride remained at the junction of the two liquids and there was no need to filter it. The aqueous layer was separated, united with the washings from the benzene layer, and titrated with $N/80$-potassium thiocyanate.

Variations in the concentrations were limited by the impossibility of making up cold alcoholic solutions of picryl chloride stronger than $M/20$.

The unit employed throughout is the equivalent of 1 c.c. of $M/40$-solution for 10 c.c., *i.e.*, one four-hundredth of a mol. per litre.

When the reaction was carried on for a sufficient length of time at 23·2° in dry or absolute alcohol, a point was reached after about 3 hours at which the titrations were practically constant. In most cases, the equilibrium point was obtained by taking measurements 10 hours after mixing. Beyond this stage, a very slow formation of chloride ion could be observed from titrations taken at daily intervals.

The equilibrium constant $K = k_2/k_1$ [see (10)] was calculated in the forward reaction from the equation

$$K = (a - x)(b - x)/x,$$

the mean value obtained being 2·28 at 23·2°.

Measurements were also made of the rate of decomposition of picrylpyridinium chloride. Only very dilute solutions could be used owing to the relative insolubility of this compound in cold

alcohol. Calculation of the initial velocity showed fairly good agreement with the result obtained for k_2 from the equilibrium constant. From the reverse reaction

$$K = [\text{Pyridine}][\text{Picryl chloride}]/[\text{Picrylpyridinium chloride}]$$

the mean value at 23·2° was 2·20.

From the initial velocity coefficients obtained from the opposing reactions, calculated from the simple bimolecular and unimolecular formulæ, respectively, one finds, *e.g.*,

$$K = k_2/k_1 = 0{\cdot}00774/0{\cdot}00375 = 2{\cdot}07,$$

the average value being 2·05.

Owing to considerations of space, only the necessary typical series of measurements are given and the remainder are summarised in Table C. Time is in minutes in all cases.

Tables A.

Reaction between Pyridine and Picryl Chloride.

I. $a = 5$, $b = 7{\cdot}5$. Solvent: Absolute alcohol. Temperature: 23·2°.

t.	x.	$k_1 \times 10^5$.
11	1·14	368
20	1·76	369
30	2·23	362
40	2·53	375
60	2·83	348
90	3·14	353
	Mean	364

II. $a = 5$, $b = 5$. Solvent: Absolute alcohol. Temperature: 23·2°.

t.	x.	$k_1 \times 10^5$.
10	0·79	361
20	1·23	359
30	1·58	359
40	1·80	347
60	2·13	348
90	2·32	311
600	2·60	—
	Mean	329

III. $a = 5$, $b = 5$. Solvent: Dried alcohol + 2 c.c. of water in 100 c.c. Temperature: 23·2°.

t.	x.	$k_1 \times 10^5$.	$*k \times 10^5$.
10	0·81	406	422
20	1·29	389	416
30	1·62	376	428
60	2·20	385	469
100	2·49	—	—
	Mean	394	439

IV. $a = 5$, $b = 5$. Solvent: Dried alcohol + 6 c.c. of water in 100 c.c. Temperature: 23·2°.

t.	x.	$*k \times 10^5$.
10	1·01	530
20	1·49	552
33	1·93	593
43	2·11	588
600	3·90	—
	Mean	566

* Calculated from the integrated form of equation (4).

V. $a = 5$, $b = 5$. Solvent: Absolute alcohol. Temperature: 33·3°.

t.	x.	$k_1 \times 10^5$.
10	1·21	775
20	1·75	777
30	1·94	712
40	2·04	665
250	2·22	—
	Mean	732

VI. $a = 5$, $b = 5$. Solvent: Absolute alcohol. Temperature: 49·1°.

t.	x.	$k_1 \times 10^5$.
10	1·45	1480
20	1·60	1290
30	1·63	1060
65	1·65	—
	Mean	1320

An experiment at 39·7° gave $k_1 \times 10^5 = 827$.

TABLE B.

Decomposition of Picrylpyridinium Chloride.

Solvent: Absolute alcohol. Tempera ure: 23·2°.

t	0	25	70	300
c	3·52	2·90	2·35	1·60

This gives an initial value for $k_2 \times 10^5$ of 751, and a second experiment, using an initial concentration of 2·21, gave 786.

TABLE C.

(Temperature throughout, 23·2°. The solvent was ordinary alcohol in all cases except that marked †, in which anhydrous alcohol was used.)

		$k_1 \times 10^5$.				$k_1 \times 10^5$.	
a.	*b*.	Range.	Mean.	*a*.	*b*.	Range.	Mean.
4·85	5·00	339—299	315	10·00	7·58	314—269	290
9·90	5·00	303—259	282	†5·00	5·00	355—301	312
4·70	10·00	308—263	286	10·00	10·00	326—257	300
5·00	5·05	316—274	309	7·50	7·40	337—274	312
7·50	7·58	321—250	288	7·50	5·00	310—271	285
7·50	10·10	362—279	321	4·93	7·40	342—291	331
4·00	20·20	354—315	323*				

* Based on integrated form of equation (4).

Summary.

1. The reaction between picryl chloride and pyridine in alcoholic solution is bimolecular and results in the slow formation of an ionised additive compound, picrylpyridinium chloride. The quantity of this compound produced depends on the concentration of the reactants and on the temperature.

2. The equilibrium reaction is accompanied by slow side reactions in which pyridine picrate and ethyl picrate are produced, the former being considerably accelerated by the presence of water.

3. A very slow reaction—only apparent after a few days—takes place between picryl chloride and pyridine picrate, with the result that picrylpyridinium picrate crystallises from the solution.

4. The evidence adduced for the formation of an ionised additive compound points to the probability of the formation of similar substances when picryl halogen compounds react with other aromatic amino-bases, at any rate as a preliminary to other reactions which may take place.

The author wishes to express his indebtedness to the authorities of the Chelsea Polytechnic for the facilities enjoyed, and particularly to Dr. J. C. Crocker for his direction and advice.

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CCCXXII.—*An Experimental Study of Protective Colloids. Part I. The Influence of Concentration.*

By Samuel Sugden and Montague Williams.

Although cases of colloidal protection have been known and used in industry from the earliest times, the first quantitative study of the phenomenon is to be found in the work of Zsigmondy (*Z. anal. Chem.*, 1901, **40**, 697), in which the relative protective action of a number of substances was measured by the weight required to inhibit the precipitation of a standard gold sol by a 10% sodium chloride solution. Later Billitzer (*Z. physikal. Chem.*, 1905, **51**, 129) found that in low concentrations gelatin gave anomalous results: when a small amount of gelatin was added to an electronegative colloid, precipitation by electrolytes was facilitated; on the other hand, gelatin in larger amounts hindered precipitation. In the case of an electropositive colloid, however, gelatin hindered precipitation at all concentrations.

Loeb (*J. Gen. Physiol.*, 1923, **5**, 479) investigated the concentrations of different salts required to precipitate suspensions of "gelatin-coated collodion particles" and found that they were practically identical with the concentrations of the same salts required for the salting out of gelatin from aqueous solutions. He stated that "neither effect showed any relation to the critical double layers surrounding the particles," and concluded that "protective colloids must be capable of forming a durable film on the surface of the suspended particles, and the molecules constituting the film must have a higher attraction for the molecules of the solvent than for each other; in other words, they must possess true solubility."

Further, Gann (*Koll.-Chem. Beih.*, 1916, **8**, 252) found that gelatin and other proteins precipitated a red gold sol, and later, Kermack and Wright (*Biochem. J.*, 1923, **17**, 635) studied the precipitation of a gum benzoin sol by gelatin over a wide range of values of p_H and found that precipitation occurred on the acid side of the isoelectric point of gelatin ($p_H = 4{\cdot}7$) and protection on the alkaline side. Rideal (*Proc. Camb. Phil. Soc.*, 1924, **22**, 101) describes experiments in which very dilute gelatin solutions were added to a gold sol which was made acid or alkaline in separate experiments. Precipitation occurred at $p_H < 5$, and protection with the alkaline solutions. Rideal concludes from a discussion of these and other data that these anomalies in the behaviour of protective colloids are to be ascribed to idiosyncrasies in the specific adsorbing power for particular ions of the particles of sol and protective colloid.

Kermack and MacCullum (*Proc. Roy. Soc. Edin.*, 1924–25, **45**,

71) investigated the influence of gelatin on the stability of cholesterol suspensions over a wide range of acidities and found two zones of stable sols, one with high concentrations of gelatin in which the particles are positively charged, and the other with low concentrations in which the cholesterol particles are negatively charged.

Boutaric and Perreau (*Compt. rend.*, 1925, **181**, 511) have investigated the interaction of a number of negative colloids and protective colloids and have found that " in the majority of cases the addition of small quantities of protective colloids makes the sol more sensitive to the action of electrolytes; if larger quantities of colloid are added, the increase in sensitivity gradually diminishes to zero; if larger quantities of colloid are added, a protective action is more and more clearly shown; very large amounts bring about coagulation of the sol."

Many more observations of anomalous protective action and of sensitisation could be quoted, but, from a general survey of the literature, it appears probable that two distinct phenomena are concerned, according as the protective colloid is present in low or in high concentration. We have studied the effect of varying the concentrations both of protective colloid and of electrolyte; we have worked also with dispersoid colloids which could be obtained in considerable concentration, *e.g.*, arsenious sulphide and aluminium hydroxide, and have therefore been able to vary the concentration of the sol over a considerable range. It will be seen from the results which follow that, when the interaction of a system dispersoid colloid–emulsoid colloid–electrolyte is viewed broadly, all the systems studied show a remarkable similarity. Sensitisation and protection of the dispersoid colloid appear to be particular aspects of the reaction regarded as a whole and either may be brought about at will by a variation in concentration of the two types of colloid.

Experimental.

Arsenious sulphide sol was chosen as a typical negatively-charged colloid. It was prepared in the usual manner by making arsenious oxide into a paste and slowly adding it to boiling distilled water; after boiling for some time, the solution was allowed to cool, and saturated with sulphuretted hydrogen, which had been freed from acid vapours and spray by passage through two wash-bottles and a U-tube filled with cotton-wool; the sol was freed, as far as possible, from sulphuretted hydrogen by the prolonged passage of hydrogen and, after filtering, was bottled and left to " age " for several weeks. The concentration of the sols was determined by oxidation and precipitation as magnesium ammonium arsenate.

As an example of a positively-charged colloid, aluminium hydr-

oxide was used. This was prepared by dissolving aluminium chloride in dilute hydrochloric acid, adding a considerable quantity of distilled water, and precipitating the hydroxide by ammonia. The gelatinous precipitate was thoroughly washed, transferred to a flask, and boiled for some time with distilled water to which a few drops of $N/20$-hydrochloric acid were occasionally added. After filtering, the sol was bottled and left to "age." Its strength was determined by coagulation with ammonium chloride and ignition of the precipitated hydroxide.

Coignet's "Gold Label" gelatin (ash content, 0·9%) was used as the first protective colloid. During the preliminary work, it became clear that the gelatin solutions prepared on different days varied in properties, and it was found necessary to standardise the preparation and to make up and mix the whole of the series of mixtures (usually 144) on the same day with the same gelatin solution. The method of preparation was to allow a weighed quantity of the gelatin to soak in distilled water for 24 hours; warming in a water-bath at about 60° for 10 minutes then made a satisfactory solution, which was diluted to the required strength.

Barium chloride, sodium chloride, and sodium sulphate were used as precipitating electrolytes. In each case it was found convenient to make up a series of stock solutions, the normalities of which decreased in geometrical progression.

The points of a system which had to be fixed first were (1) the concentration of electrolyte necessary to precipitate the sol in the absence of protective colloid, (2) the concentration of protective colloid required to cause mutual precipitation between the two colloids in the absence of electrolyte, and (3) the concentration of protective colloid beyond which mutual precipitation ceased. With these datum points, it was possible to judge approximately the most suitable ranges of concentration of electrolyte and protective colloid for investigation.

During preliminary work, the protective colloid was added to the sol and the precipitating electrolyte added later; this, however, gave unsatisfactory results owing to the masking of the protecting action by mutual precipitation phenomena. Afterwards the protective colloid was therefore always added to the electrolyte before mixing the three reactants together.

A number of test-tubes (usually 288) were steamed, washed out with distilled water, and left to drain thoroughly in a series of stands. When the test-tubes were dry, 5 c.c. of arsenious sulphide sol were pipetted into each in alternate rows. The sodium chloride and gelatin, giving together a total volume of 5 c.c. in each tube, were then pipetted into the remainder so that each horizontal row had

the same concentration of electrolyte and each vertical row the same concentration of gelatin. To effect mixing, the gelatin and sodium chloride were poured into the sol, the whole was poured back again and then finally transferred to the test-tube which originally contained the sol. After being corked up, the mixtures were allowed to stand for 24 hours. Precipitation was estimated by allotting numbers as follows: Complete precipitation, 4; nearly complete precipitation, 3; half-precipitation, 2; definite turbidity, 1; and no turbidity, 0.

The results then appeared as in Table I.

TABLE I.

Final conc. of electrolyte.	Precipitation number.											
$8N/5$	4	4	4	4	4	4	2	0	0	0	0	0
$4N/5$	4	4	4	4	4	4	2	2	2	0	0	0
$2N/5$	4	4	4	4	4	4	4	2	1	1	0	0
$N/5$	4	4	4	4	4	4	4	4	4	2	0	0
$N/10$	4	4	4	4	4	4	4	4	4	4	2	0
$N/20$	4	4	4	4	4	4	4	4	4	4	2	0
$N/40$	1	4	4	4	4	4	4	4	4	4	2	0
$N/80$	0	2	4	4	4	4	4	4	4	4	2	0
$N/160$	0	0	4	4	4	4	4	4	3	1	0	0
$N/320$	0	0	2	4	4	4	4	4	2	0	0	0
$N/640$	0	0	0	4	4	4	4	4	2	0	0	0
$N/1280$	0	0	0	4	4	4	4	4	0	0	0	0
Final conc. of gelatin (%).	0·001	0·002	0·003	0·004	0·005	0·006	0·007	0·008	0·009	0·010	0·011	0·012

To save space and facilitate the comparison of the data obtained for different systems, full details are given for this sol only, and all the results are plotted in Fig. 1. In plotting the diagrams, results denoted by 3 are shown as complete precipitation (shaded areas), and those recorded as 1 are shown as no precipitation (clear areas).

The systems first investigated and shown in Figs. 1, 2, and 3 are:

FIG. 1.

(*a*) Arsenious sulphide sol (0·290 g./l.) + gelatin + sodium chloride.
(*b*) „ „ „ (0·581 g./l.) + „ + „ „
(*c*) „ „ „ (1·173 g./l.) + „ + barium chloride.
(*d*) „ „ „ (4·650 g./l.) + „ + „ „

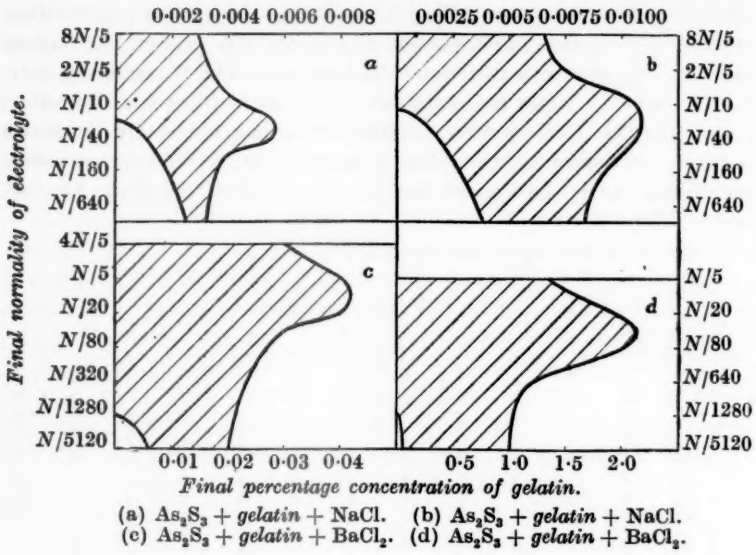
FIG. 2.

(*a*) Aluminium hydroxide sol (0·770 g./l.) + gelatin + sodium chloride.
(*b*) „ „ „ (0·770 g./l.) + „ + sodium sulphate.

FIG. 3.

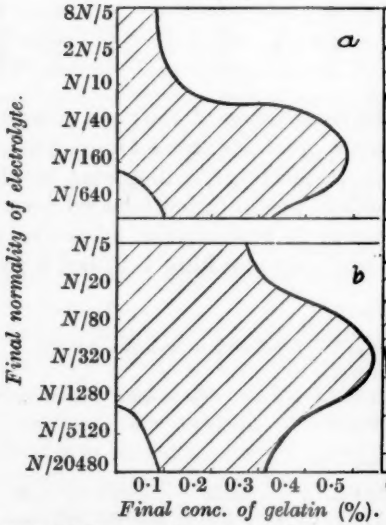
(*a*) Arsenious sulphide sol (0·581 g./l.) + normal blood serum + sodium chloride.
(*b*) „ „ „ (0·581 g./l.) + syphilitic blood serum + sodium chloride.

FIG. 1.



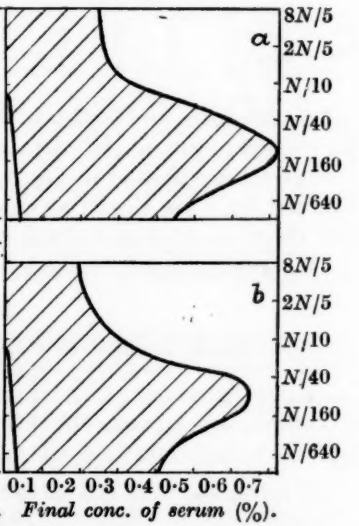
(a) As_2S_3 + *gelatin* + NaCl. (b) As_2S_3 + *gelatin* + NaCl.
(c) As_2S_3 + *gelatin* + $BaCl_2$. (d) As_2S_3 + *gelatin* + $BaCl_2$.

FIG. 2.



(a) $Al(OH)_3$ + *gelatin* + NaCl.
(b) $Al(OH)_3$ + *gelatin* + Na_2SO_4.

FIG. 3.



(a) As_2S_3 + *normal serum* + NaCl.
(b) As_2S_3 + *syphilitic serum* + NaCl.

With one exception, all the experiments were carried out at room temperature. In system 1(*d*) the tubes were heated to 37° for 24 hours before reading, since such high concentrations of gelatin were

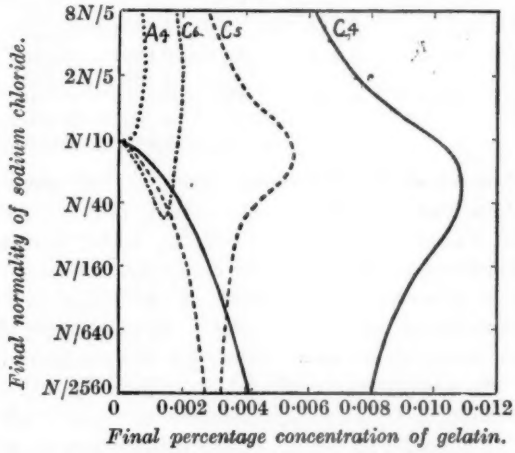
needed that a jelly was formed in many of the tubes at room temperature.

Discussion of Results.

We shall use the term " dispersoid sol " to designate the colloid the concentration of which is kept constant through a series of mixtures (arsenious sulphide, aluminium hydroxide) whilst the term " protective colloid " is used for the one the concentration of which is varied (gelatin, blood-serum).

It is immediately apparent from the diagrams that all the systems investigated show a great similarity in behaviour. The characteristic features are: (1) Small amounts of protective colloid produce a greater sensitivity towards electrolytes; (2) this sensitivity increases progressively until the two colloids precipitate one another even in

FIG. 4.



the absence of electrolyte; (3) at higher concentrations of protective colloid, a protective effect is found, but the curves exhibit a curious shape with a definite proboscis at certain concentrations of electrolyte.

These characteristic features are found in all the diagrams, although every possible variable has been changed. For the negative arsenious sulphide sols of varying concentrations, the same type of curve is given with univalent and bivalent positive precipitating ions and with gelatin and blood-serum as protective colloids. (Blood-serum was used in connexion with the Sachs-Georgi test; an account of further experiments in this reaction will be published shortly in another journal.) Similarly, the positive sol, aluminium hydroxide, with gelatin as protective colloid, gives the same type of curve with both uni- and bi-valent negative precipitating ions.

The principal effect of increasing the concentration of the sol

appears to be to shift the curve towards the region of greater concentrations. This is shown clearly in Fig. 4, which gives the curve for a series of sols obtained by diluting the strongest sols examined. An interesting quantitative relationship is revealed when the concentration of the sol is compared with the amount of gelatin which causes maximum precipitation. For this latter quantity, we have taken the concentration indicated by the middle point of the zone of precipitation by gelatin alone. As Table II shows, for three different sols the concentration of gelatin is roughly proportional to the concentration of the sol when the latter falls below about 1 g. per litre.

TABLE II.

Sol.	As_2S_3 (g./l.).	Gelatin (g./l.).	Ratio Gelatin: As_2S_3.	Sol.	As_2S_3 (g./l.).	Gelatin (g./l.).	Ratio Gelatin: As_2S_3.
A_1	0·581	0·060	0·103	C_1	4·650	5·03	1·13
A_2	0·290	0·029	0·100			5·25	1·18
A_3	0·145	0·015	0·103	C_2	2·325	1·50	0·645
A_4	0·072	?	—	C_3	1·162	0·150	0·129
B_1	1·173	0·13	0·111	C_4	0·581	0·060	0·103
				C_5	0·290	0·030	0·103
				C_6	0·145	0·015	0·103

This result is somewhat surprising, since the sols were prepared under widely varying conditions. For sols A_1 and B_1, the whole of the arsenious oxide was dissolved in the water before passing sulphuretted hydrogen; to attain the concentration of sol C_1, however, it was necessary to add a paste of the oxide and water at intervals during the passage of the gas. Nevertheless, this sol on dilution gives precisely the same values for the amounts of gelatin which cause the maximum precipitation. Sols C_2, C_3, etc., were prepared by diluting C_1 and were allowed to "age" for 3 weeks before use. It appears, therefore, that a diluted arsenious sulphide sol on standing reaches a steady state in so far as precipitation is concerned. The numerical value of the ratio gelatin/arsenious sulphide is of interest. The maximum precipitation is produced by a quantity of gelatin that is roughly one-tenth of the weight of the arsenious sulphide present. This is in harmony with the view that the reaction is one between small aggregates of gelatin molecules and large aggregates of the sulphide.

The general effect of dilution of the dispersoid sol on the form of the diagram is shown in Fig. 4. The concentration of the sol has little or no influence on the amount of electrolyte which produces coagulation in the absence of gelatin. All the sols of arsenious sulphide are precipitated by $N/10$- to $N/20$-sodium chloride (Figs. 1*a*, 1*b*, and 4) and by $N/1280$-barium chloride (Figs. 1*c* and 1*d*).

The position of the "nose" varies systematically with the con-

centration of the sulphide; this is shown for the weaker sols in Fig. 4. Table III gives the position of the tip of the nose for the complete C-series of sols.

TABLE III.

		Position of nose.				Position of nose.	
		NaCl	Gelatin			NaCl	Gelatin
Sol.	As_2S_3 (g./l.).	conc.	(g./l.).	Sol.	As_2S_3 (g./l.).	conc.	(g./l.).
C_1	4·65	$N/60$	19·5	C_4	0·581	$N/30$	0·108
C_2	2·325	$N/40$	14·0	C_5	0·290	$N/15$	0·055
C_3	1·162	$N/30$	0·75	C_6	0·145	$2N/5$	0·021

The most remarkable feature of these results is the great extension of the zone of precipitation into solutions of high gelatin content in sols C_1 and C_2.

It appears probable from our results that the behaviour of protective colloids in general may be represented by a diagram of the form shown in Fig. 1, etc. The narrowing of the zone of precipitation as the concentration of dispersoid colloid is lowered, and the ultimate disappearance of a zone of mutual coagulation in the absence of electrolyte are clearly shown in Fig. 4; with very dilute sols the sensitising effect of the protective colloid will not manifest itself, and the relation between sensitisation and protection will be obscured. This may account for the results of Billitzer (*loc. cit.*) and other workers who did not observe precipitation by gelatin alone.

The results of Kermack and MacCullum (*loc. cit.*) give a diagram somewhat similar to that found in the present work when hydrogen ion is regarded as the precipitating electrolyte. From p_H 4·8 to p_H 13 no coagulation was found, and from p_H 13 to p_H 15 a zone of coagulation by alkalis occurred, which, of course, has no counterpart in our curves. These workers found also that sodium chloride broadened the zone of mutual coagulation of the two colloids, which is again in agreement with our results.

The types of curve obtained in these experiments suggest at once a comparison with the results of Billitzer (*loc. cit.*) on the mutual precipitation of oppositely charged colloids when present in amounts sufficient to neutralise one another. The precipitation of both positive and negative sols by gelatin might then be ascribed to the amphoteric character of this colloid (compare Rideal, *loc. cit.*). We suggest this explanation tentatively, but intend to examine other systems and to study the sign of the electrical charge in the neighbourhood of the zone of coagulation in order to test this hypothesis. In particular, the characteristic bulge or proboscis which occurs in all the diagrams seems to indicate that some factor other than simple neutralisation of the sol is concerned.

*Summary.**

(1) Simultaneous variation of the concentrations of protective colloid and electrolyte in a series of systems, dispersoid colloid–protective colloid–electrolyte, has revealed an area of coagulation of characteristic shape.

(2) In dilute solutions, protective colloids sensitise the sol and at suitable concentrations cause precipitation in the absence of more than traces of electrolytes.

(3) For arsenious sulphide sols with concentrations of less than 1 g. per litre the amount of gelatin which causes maximum precipitation is proportional to the arsenious sulphide content.

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CCCXXIII.—*Mercuration of Some Alkylphenols and Alkylphenolaldehydes.*

By THOMAS ANDERSON HENRY and THOMAS MARVEL SHARP.

IN previous papers (J., 1922, **121**, 1055; 1924, **125**, 1049) the authors have described the mercuration of the hydroxybenzaldehydes and certain of their nitro-derivatives and have shown that the bactericidal action of the organo-mercury compounds formed is not entirely dependent on the number of mercury residues present, but is largely influenced by the configuration of the organic part of the molecule; thus, 2-hydroxymercuri-3-hydroxybenzaldehyde (Hg, 59·1%) is 2·5 times as toxic to *Bacillus typhosus* as 3 : 5-dihydroxymercuri-2-hydroxybenzaldehyde (Hg, 72·2%) (Henry, Sharp, and Brown, *Biochem. J.*, 1925, **19**, 513). The former is, in fact, a very active bactericidal agent and has also marked spirochæticidal properties, and solutions in oil of its acyloxy-derivatives are now being used successfully in India in the treatment of cases of leprosy complicated by syphilis.

* It has been suggested that changes in p_H might influence the phenomena described in this paper (compare Kermack and Wright, *loc. cit.*). Since, however, the sols used and the protective colloids are buffers and the precipitating electrolytes are neutral and unhydrolysed, the p_H of the solutions must have been nearly constant throughout each series; no appreciable influence in the sensitising or protecting power of the gelatin is therefore to be expected. Variation of p_H, as in the work of Kermack and his co-workers, and of the concentration of the ions $Na^{\cdot}$, $Ba^{\cdot\cdot}$, Cl', SO_4'' in the work described in the present paper gives in all cases similar results, so it does not appear necessary to postulate that the hydrogen ion plays a special part in these reactions.

It seemed desirable to ascertain whether the bactericidal action could be increased by the introduction of alkyl groups, since it is known that up to a certain point the *C*-alkylphenols show increasing bactericidal action with increasing weight of the substituent alkyl group.

We selected for investigation *p-tert.*-butyl- and *p-iso*amyl-phenols, carvacrol, and thymol, and one aldehyde derived from each of these.

Little has been done previously on the mercuration of alkylphenols and nothing on the mercuration of alkylphenolaldehydes. Dimroth has shown that *p*-cresol (*Ber.*, 1902, **35**, 2856) and thymol (*ibid.*, 2864) both yield mono- and di-mercurated derivatives, and other workers have investigated the same substances. *p-tert.*-Butyl- and *p-iso*amyl-phenols are now found to behave similarly, yielding both mono- and di-substituted mercury derivatives. The positions of the two mercuri-groups in the latter are shown to be in both cases ortho to the hydroxyl groups, since on treatment with cold nitric acid *o*-dinitro-compounds are formed. The constitution of the monomercuri-compounds of these two phenols follows from those of the disubstituted derivatives, and similarly the monomercuri-derivatives of the corresponding aldehydes are shown to be 2-hydroxy-3-acetoxymercuri-5-*tert.*-butylbenzaldehyde and 2-hydroxy-3-acetoxymercuri-5-*iso*amylbenzaldehyde, respectively.

Carvacrol would be expected to yield three products, *viz.*, the 4 : 6-diacetoxymercuri-, 4-acetoxymercuri-, and 6-acetoxymercuri-derivatives, since thymol yields the three analogous substances (Mameli and Mameli-Manessier, *Gazzetta*, 1922, **52**, 1), but we have only succeeded in obtaining a dimercuri- and one monomercuri-compound from carvacrol. The former is, no doubt, the expected 4 : 6-diacetoxymercuri-derivative, but the position of the mercury in the latter is difficult to determine, since coupling with benzenediazonium chloride yields a dibenzeneazocarvacrol, and treatment with bromine gives rise to polybrominated products which furnish no clue to the constitution, whilst nitric and nitrous acids give only tarry products from which no crystalline substance could be obtained. In thymol- and carvacrol-aldehydes there are only two positions available for the entry of the acetoxymercuri-residue, one meta and one ortho to the hydroxyl group. It is almost certain, therefore, that the mercury in these substances occupies the ortho-position, since meta-substituted mercuri-compounds are rarely formed, even when the directing group is one which normally causes meta-substitution (compare, however, Dimroth, *Annalen*, 1925, **446**, 148; Coffey, J., 1925, **127**, 1029; this vol., p. 637).

In the preparation of the four aldehydes used in the course of

this work a number of interesting by-products were obtained, which are being investigated.

The bactericidal action of the primary materials and of the mercury derivatives yielded by them have been kindly determined by Major Brown, C.I.E., M.B., B.Ch., bacteriologist to the Wellcome Bureau of Scientific Research. The results cannot be quoted in detail here. They indicate that the increase in bactericidal action, due to the introduction of alkyl groups into phenols, persists when the resulting alkylphenols are mercurated, and that the further introduction of an aldehyde group into the alkylphenols, as a rule, has very little influence on the bactericidal action of the final mercurated alkylphenolaldehyde.

Experimental.

Mercuration of Alkylphenols.

p-tert.-*Butylphenol.*—The *p-tert.*-butylphenol used was prepared by Liebmann's method (*Ber.*, 1882, **15**, 152, 1990); it had m. p. 99—100° and gave a crystalline benzoate, m. p. 80—81°. *p-tert.*-Butylphenol (6 g.), dissolved in alcohol (10 c.c.), and mercuric acetate (25·6 g.), dissolved in alcohol (160 c.c.) containing acetic acid (4 c.c.), were boiled together under reflux for an hour. A test portion diluted with water then dissolved completely in sodium hydroxide solution. After standing over-night, the liquid was filtered from a trace of mercurous acetate, concentrated to half-volume and then diluted with 200 c.c. of water; a white, sticky solid separated which on warming with alcohol became crystalline. After cooling, the solid was filtered off and dried to constant weight in a vacuum desiccator over sulphuric acid; it was pure 2 : 6-*diacetoxymercuri*-p-tert.-*butylphenol* (Found: C, 24·85; H, 2·7; Hg, 59·73. $C_{14}H_{18}O_5Hg_2$ requires C, 25·18; H, 2·72; Hg, 60·10%). Further quantities of this substance were obtained by concentration of the mother-liquors and repetition of the above treatment; yield 23·35 g. The substance melts at 224° (decomp.) and is readily soluble in ordinary organic solvents. The acetoxymercuri-groups were shown to be in the 2- and 6-positions by treating the product with ice-cold, concentrated nitric acid, whereupon there was formed in good yield 2 : 6-dinitro-*p-tert.*-butylphenol, m. p. 97—98° (Found: C, 50·05; H, 5·14. Calc.: C, 50·00; H, 5·04%). This m. p. was not depressed on admixture with a specimen prepared by the nitration of *p-tert.*-butylphenol (Studer, *Annalen*, 1882, **211**, 242). If the temperature is allowed to rise during this reaction the main product is picric acid.

To obtain a monomercurated product, *p-tert.*-butylphenol (6 g.; 2 mols.) and mercuric acetate (6·4 g.; 1 mol.), dissolved in 50% alcohol containing a little acetic acid, were mixed and left at room temperature for 20 hours; a test portion then dissolved in sodium hydroxide. After 3 days, a good crop of white needles had separated; this was filtered off and washed with alcohol and ether (yield 2·53 g.). It consisted of a mixture rich in the monomercurated substance. On concentrating the filtrate, some unchanged butylphenol passed over and a clear yellow oil separated which solidified on standing. This solid was steam-distilled to remove butylphenol and then dried on a porous tile (3·6 g.). It crystallised from ligroin, saturated with acetic acid, in beautiful, colourless, shining plates, m. p. 180° (Found: C, 35·1; H, 4·19; Hg, 49·2. $C_{12}H_{16}O_3Hg$ requires C, 35·25; H, 3·95; Hg, 49·1%). This substance is 2-*acetoxymercuri*-p-tert.-*butylphenol*, the constitution of which follows from that of the dimercuri-compound, since the 2- and 6-positions are identical.

p-iso*Amylphenol.*—*p-iso*Amylphenol, m. p. 95° (1 mol.), prepared by Liebmann's process (*loc. cit.*), and mercuric acetate (2 mols.) dissolved in the minimum amount of alcohol containing a little acetic acid, were boiled together under reflux for 2 hours. The solution was filtered from a little mercurous acetate, concentrated somewhat, and left to cool. A white, crystalline solid separated and more was obtained on further concentration, the yield being nearly quantitative. This substance is readily soluble in alcohol, acetic acid, ethyl acetate, or chloroform, and in benzene containing a little acetic acid. It crystallises from acetic acid in shining prisms, containing 1 mol. of the solvent; m. p. 123—125° (Found: C, 27·38, 27·33; H, 3·33, 3·27; Hg, 53·98. $C_{15}H_{20}O_5Hg_2,C_2H_4O_2$ requires C, 27·52; H, 3·26; Hg, 54·1%). On treatment with twice its weight of ice-cold, concentrated nitric acid, the mercury is removed with the formation of 2 : 6-dinitro-*p-iso*amylphenol, m. p. 64—66°, not depressed after admixture with a specimen prepared by the method of Anschütz and Rauff (*Annalen*, 1903, **327**, 211). The *potassium* salt forms red plates with a coppery lustre (Found: K, 13·27. Calc.: 13·38%). As in the case of *p-tert.*-butylphenol, picric acid is formed if the temperature is allowed to rise during this reaction. The mercury compound is therefore 2 : 6-*diacetoxymercuri*-p-iso*amylphenol.*

A monomercuri-compound was obtained by mixing cold 50% alcoholic solutions of *p-iso*amylphenol (2 mols.) and mercuric acetate (1 mol.). After 26 hours the reaction was complete; the alcohol was removed by distillation and the residual oil was steam-distilled;

during this operation the oil solidified, and when no more of the phenol passed over the solid was filtered off and crystallised, first from acetic acid and then from benzene containing about 1% of acetic acid. White, crystalline flakes of 2-*acetoxymercuri*-p-iso-*amylphenol*, m. p. 176—177° (decomp.), were thus obtained (Found: C, 36·7; H, 4·4; Hg, 47·64. $C_{13}H_{18}O_3Hg$ requires C, 36·9; H, 4·3; Hg, 47·44%). It is soluble in the common organic solvents. The constitution follows from that of the dimercuri-compound.

Carvacrol.—The carvacrol used was extracted from Cyprus origanum oil (Pickles, J., 1908, **93**, 862). Solutions of carvacrol (1 mol.) and mercuric acetate (2 mols.) in 50% alcohol were boiled together under reflux for 15 minutes; a test portion diluted with water then dissolved in sodium hydroxide. On cooling a colourless, crystalline substance was obtained. On concentrating the filtrate a pale yellow oil separated; the mother-liquors were poured off and the oil crystallised on warming with alcohol. The solid was filtered, the alcoholic filtrate added to the previous mother-liquors, and the above process repeated. In this way eight crops of crystals were obtained of which the fourth and sixth were identified as mercurous acetate. From 18 g. of carvacrol 61·3 g. of crude mercury compound were obtained. The first two crops (34 g.) were almost pure mono-acetoxymercuricarvacrol, whilst crops 3, 5 and 7 (21·8 g.) were nearly pure diacetoxymercuricarvacrol. Crop 8 (5·5 g.) consisted of a mixture of the two mercury compounds. One crystallisation of crops 1 and 2 from alcohol furnished pure *acetoxymercuricarvacrol* as short, highly refractive, colourless rods (decomp. at 196°) (Found: C, 34·96; H, 4·0; Hg, 49·08. $C_{12}H_{16}O_3Hg$ requires C, 35·25; H, 3·95; Hg, 49·1%). Similarly crops 3, 5 and 7 crystallised from alcohol and yielded pure *diacetoxymercuricarvacrol*, as colourless, well-formed prisms, which softened at 190° and decomposed at 215° (Found: C, 25·13; H, 2·89; Hg, 60·2. $C_{14}H_{18}O_5Hg_2$ requires C, 25·18; H, 2·7; Hg, 60·1%). For the orientation of these mercury compounds they were severally coupled with benzenediazonium chloride in alkaline solution, Dimroth (*Ber.*, 1902, **35**, 2853) having shown that when the mercuri-residue occupies the para-position to a hydroxyl group, the mercury is removed from the nucleus, its place being taken by a benzeneazo-group, whilst mercuri-residues in the ortho-position remain. Unfortunately, in this case both the mercuri-groups were removed and the product was *op*-di-benzeneazocarvacrol, which crystallised from alcohol in dark red-brown needles, m. p. 163° (corr.). The same product is obtained by coupling carvacrol with benzenediazonium chloride in alkaline solution (von Auwers and Michaelis, *Ber.*, 1914, **47**, 1295; these

authors give m. p. 158°). Since no case is known in which a mercuri-residue enters the benzene ring *meta* to a hydroxyl group, it is highly probable that the dimercurated product is 4 : 6-diacetoxymercuricarvacrol (HO in 1), which also makes it analogous with the 2 : 4-diacetoxymercurithymol : the monomercurated carvacrol may have the mercuri-residue in either the 4- or the 6-position.

Mercuration of Alkylphenolaldehydes.

2-*Hydroxy*-5-tert.-*butylbenzaldehyde*.—This substance has been prepared by the Reimer-Tiemann process (Dains and Rothrock, *Amer. Chem. J.*, 1894, **16**, 635) but we were only able to obtain minute yields by this method. For these experiments, it was prepared by condensing *p-tert.*-butylphenol with formaldehyde (B.P. 161679/1920), a process which usually furnishes substances with the aldehyde group in the para-position to the hydroxyl group. In this case, the para-position is occupied and the aldehyde group enters the ortho-position. The yield of pure aldehyde, b. p. 138—140°/12 mm., was 46% of the theoretical. It gave a phenylhydrazone, bright yellow plates, m. p. 184° (Found : C, 76·19; H, 7·5; N, 10·4. Calc. for $C_{17}H_{20}ON_2$: C, 76·1; H, 7·5; N, 10·4%).

2-Hydroxy-5-*tert.*-butylbenzaldehyde and mercuric acetate in molecular proportions, dissolved in alcohol containing acetic acid, were boiled under reflux for 15 minutes, a test portion then dissolving completely in sodium hydroxide. On cooling, mercuric acetate separated and on reheating the mercury compound was again formed at once. The hot solution was therefore poured into a large volume of water and the resulting white precipitate was filtered off at once. After drying in a vacuum desiccator, the substance was crystallised from alcohol containing a very little acetic acid; white, needle-shaped crystals separated, m. p. 220°, but from the crystallisation of 3·8 g. only 1·93 g. of the mercury compound could be obtained (Found : C, 35·6; H, 3·8; Hg, 45·84, 45·96. $C_{13}H_{16}O_4Hg$ requires C, 35·7; H, 3·7; Hg, 45·92%). This compound can only be 2-*hydroxy*-3-*acetoxymercuri*-5-tert.-*butylbenzaldehyde*. A yield of 73% of the theoretical can be obtained by heating together molecular proportions of the aldehyde and mercuric acetate on the water-bath for 2 hours without solvent. The liquid formed is then extracted with a hot mixture of benzene and ligroin containing acetic acid, filtered from mercurous acetate, and the filtrate set aside to cool, the mercuri-compound then separating.

2-*Hydroxy*-5-iso*amylbenzaldehyde*.—This substance has not been described previously. It was obtained by condensing *p-iso*amyl-

phenol with formaldehyde and is a liquid boiling at 165—168°/17 mm. The yield of pure aldehyde was 35% of the theoretical (Found: C, 74·6; H, 8·4. $C_{12}H_{16}O_2$ requires C, 74·96; H, 8·4%): *semicarbazone*, white needles from alcohol, m. p. 222° (Found: C, 62·3; H, 7·55; N, 17·1. $C_{13}H_{19}O_2N_3$ requires C, 62·55; H, 7·69; N, 16·89%). The *phenylhydrazone* crystallises from alcohol in white plates, which soon turn yellow, m. p. 177—178° (Found: C, 76·6; H, 8·0; N, 10·3. $C_{18}H_{22}ON_2$ requires C, 76·52; H, 7·85; N, 9·97%).

The mercuration of this aldehyde in alcoholic solution gave only a small yield of mercury compound, and the same phenomenon of demercuration was observed on cooling the alcoholic solution (see above). A much better yield was obtained by heating together equimolecular proportions of 2-hydroxy-5-*iso*amylbenzaldehyde and mercuric acetate on a water-bath in the absence of any solvent. After heating for 4 hours, a dark liquid was obtained which contained a trace of mercurous acetate but was otherwise completely soluble in sodium hydroxide. The liquid was extracted with ligroin, filtered from mercurous acetate, and the solution left to cool; bundles of white needles, m. p. 134—135°, were then obtained (yield 85% of theoretical) (Found: C, 37·27; H, 3·94; Hg, 44·6. $C_{14}H_{18}O_4Hg$ requires C, 37·27; H, 4·0; Hg, 44·5%). This compound must be 2-*hydroxy*-3-*acetoxymercuri*-5-iso*amylbenzaldehyde*.

4-*Hydroxy*-3-*methyl*-6-iso*propylbenzaldehyde* (p-*carvacrolaldehyde*).—Molecular proportions of *p*-carvacrolaldehyde, prepared by Adams and Montgomery's form of the Gattermann process (*J. Amer. Chem. Soc.*, 1924, **46**, 1519), and mercuric acetate, dissolved in alcohol containing acetic acid, were boiled under reflux for 1½ hours; a test portion well diluted with water then dissolved completely in sodium hydroxide solution. The solution was filtered from a trace of mercurous acetate into excess of a 10% solution of sodium chloride. A pale cream-coloured precipitate formed (m. p. about 260°, decomp.); it was filtered, dried in a desiccator, crystallised from acetone containing one drop of hydrochloric acid, and thus obtained in small, four-sided plates, which soften and darken at about 209° and decompose indefinitely at about 260° (Found: C, 31·92; H, 3·17; Hg, 48·67. $C_{11}H_{13}O_2ClHg$ requires C, 31·95; H, 3·17; Hg, 48·54%). This substance is no doubt 4-*hydroxy*-5-*chloromercuri*-3-*methyl*-6-iso*propylbenzaldehyde*, since the only other possible position for the mercury is meta to the hydroxyl group. This compound is curiously unstable in solution; from 5·3 g. dissolved in acetone only 2·7 g. of the mercury compound could be recovered and the mother-liquors yielded unmercurated *p*-carvacrol-

aldehyde. Moreover, if the alcoholic solution of the mercuration product (which is completely soluble in sodium hydroxide) is allowed to cool before being poured into sodium chloride, mercuric acetate crystallises out. When this solution containing mercuric acetate is boiled again the whole becomes soluble in caustic alkalis (compare the mercury derivatives of the other alkylphenolaldehydes described in this paper).

A 50% yield of the corresponding 5-acetoxymercuri-derivative is obtained by heating together on a water-bath molecular proportions of *p*-carvacrolaldehyde and mercuric acetate for 1½ hours. The resulting yellow, viscous oil, containing some mercurous acetate, is extracted four times with hot ligroin to remove unchanged carvacrolaldehyde. The residue is dissolved in a small quantity of acetic acid and filtered from mercurous acetate. On cooling, colourless needles of *4-hydroxy-5-acetoxymercuri-3-methyl-6-isopropylbenzaldehyde* separate, m. p. 120°; they contain 1 mol. of acetic acid, which is not lost on drying in a vacuum desiccator (Found: C, 36·42; H, 4·17; Hg, 40·6. $C_{13}H_{16}O_4Hg,C_2H_4O_2$ requires C, 36·24; H, 4·06; Hg, 40·4%). On concentrating the acetic acid mother-liquors, demercuration takes place and mercuric acetate crystallises out.

On shaking the mercuri-compound with a solution of iodine in potassium iodide, an iodo-derivative, probably *5-iodo-4-hydroxy-3-methyl-6-isopropylbenzaldehyde*, crystallising from alcohol in long, colourless needles, m. p. 157°, is obtained in good yield (Found: I, 42·18. $C_{11}H_{13}O_2I$ requires I, 41·75%).

4-Hydroxy-2-methyl-5-isopropylbenzaldehyde (p-*thymolaldehyde*).—Molecular proportions of thymolaldehyde, prepared by Adams and Montgomery's method (*loc. cit.*), and mercuric acetate, dissolved in alcohol containing a little acetic acid, were boiled under reflux for 15 minutes, filtered from a little mercurous acetate, and left to cool. A pale, cream-coloured, crystalline solid separated and more was obtained by concentrating the mother-liquors (yield of crude substance, 94% of theoretical). This is very impure (Hg, 50·6%). It crystallises well from acetone, containing a trace of acetic acid, in colourless, hard prisms, which decompose at 185° after sintering at 179°, but it is unstable in this solvent, some of the mercury being removed with re-formation of *p*-thymolaldehyde, which is recovered from the final mother-liquors (Found: C, 36·0; H, 3·9; Hg, 46·1. $C_{13}H_{16}O_4Hg$ requires C, 35·7; H, 3·7; Hg, 45·9%). The position of the mercury in this substance has not been proved, but there can be little doubt that the compound is *3-acetoxymercuri-4-hydroxy-2-methyl-5-isopropylbenzaldehyde*, since the only other available position (6) is meta to the hydroxyl group. On treatment with a

solution of iodine in potassium iodide, the mercury is replaced by iodine with formation of an iodo-compound, which is probably 3-*iodo*-4-*hydroxy*-2-*methyl*-5-iso*propylbenzaldehyde*, crystallising from alcohol in pale yellow, octagonal prisms, m. p. 128—129° (Found: C, 43·8; H, 4·3; I, 41·8. $C_{11}H_{13}O_2I$ requires C, 43·4; H, 4·3; I, 41·75%).

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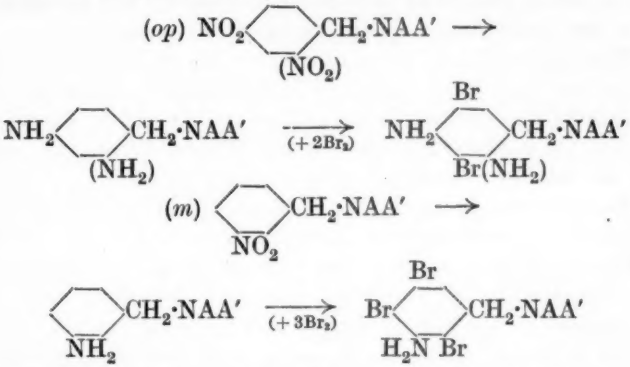
CCCXXIV.—*The Nature of the Alternating Effect in Carbon Chains. Part VIII. The Nitration of Some Benzylamine Derivatives with Special Reference to the Respective Rôles of the Ions, Salts, and Bases.*

By FRANK ROBERT GOSS, CHRISTOPHER KELK INGOLD, and IAN STUART WILSON.

IN Part III of this series (Holmes and Ingold, J., 1925, **127**, 1800) it was shown that whilst benzyl ethers and esters, $C_6H_5 \cdot CH_2 \cdot OA$, nitrate exclusively in the *op*-positions in the benzyl group, benzylamine derivatives, $C_6H_5 \cdot CH_2 \cdot NAA'$, frequently give large proportions of *m*-isomerides. The contrast between these two classes of compounds is very strongly marked, but experiments of a quantitative kind are required to enable conclusions to be drawn regarding the effect of structure on the tendency to *m*-substitution of the individual benzylamines amongst themselves, and it is in this direction that the present paper extends the previous work.

It has been found that benzylamine derivatives are not appreciably altered by cold dilute bromine solution under conditions in which aniline and its nuclear substitution products are rapidly and quantitatively brominated. We have therefore utilised Francis and Hill's method of quantitative bromination by means of acidified bromide–bromate solution (*J. Amer. Chem. Soc.*, 1924, **46**, 2498) to determine the proportion of *m*-derivative formed in the nitration of different benzylamine compounds: the mixture of isomeric nitro-compounds is first reduced to the amino-benzylamine derivatives, which are then brominated; in the simplest instance the proportion of *m*-isomeride can be directly calculated from the quantity of bromine entering the molecule since the *m*-amino-

compound can take up three atoms of bromine, whilst its *o*- and *p*-isomerides can yield only dibromo-derivatives :



The table below summarises the results obtained by this method for eleven benzylamine derivatives. In seven of the cases, more than one experiment was carried out in order to show the degree of reproducibility of the results when every effort is made to keep the conditions of nitration identical. The figures in col. 4 show that exact reproducibility is extremely difficult to attain, but the mean values (col. 5) are regarded as approximately representative of the varying tendencies to *m*-substitution in the different cases. Individual results which, not being considered typical, have been excluded from the calculation of the mean values, are shown in square brackets. Since the experimental error is expected to be similar, no matter whether the proportion of *m*-isomeride is large or small, it will in the latter case bear a correspondingly greater ratio to the values given.

Nitration of Benzylamine Derivatives.

(Reagent : Nitric Acid, *d* 1·50.)

Class.	Formula.	Temp.	Proportion of *m*-isomeride (%). Individual results.	Mean.
Quaternary salt.*	(1) $BzNEt_3^+$	−5°	85	85‡
Primary base.	(2) $BzNH_2$	0	[34], 40, 41, 43, 44, 48, 49†	44
Secondary base.	(3) Bz_2NH	0	[68], 75, 76, 76, [87]	76
Tertiary bases.	(4) Bz_3N	0	53, [60]	53
	(5) Bz_2NMe	0	52, 64	58
	(6) $BzNMe_2$	0	57, 58, 60	58
	(7) $BzNEt_2$	0	51	51
Monoacyl derivs.	(8) BzNHAc	0	6, 8	7
	(9) BzNMeAc	0	8	8
	(10) Bz_2NAc	0	23, 26	25
Diacyl deriv.	(11) BzNSuccinyl	−12	1	1

* Picrate used. † By separation.

‡ Compare *Chem. and Ind.*, 1926, **45**, 43.

The detailed descriptions of these experiments are to be found in the experimental portion, but the following notes regarding the extent to which the above data are confirmed by the actual separation of the isomerides may appropriately be given:

(1) The substitution of the quaternary salt is theoretically important, and the very large degree of *m*-substitution characteristic of benzyltriethylammonium picrate has been confirmed by the isolation of 79% of the *m*-nitro-derivative in the pure condition—*i.e.*, all but 6% of the quantity estimated to be present (p. 2450).

(2) Benzylamine is the fundamental compound of the series and its nitration has therefore been studied with particular care. Methods have been elaborated whereby the bulk of the *m*- and *p*-isomerides can be separated in the pure state, and the unseparated residue has been oxidised to the readily separable nitrobenzoic acids. In this way, the following independent estimation of the proportions of the isomerides has been made:

Ortho-, 8%; *meta*-, 49%; *para*-, 43%.

The figure for the *m*-content is included in the table given above. For the reasons given on p. 2453, Holmes and Ingold's estimate of the *m*-content is certainly too high.

(3), (8), (9), (10), and (11). Qualitative separations recorded either by Holmes and Ingold or by ourselves confirm these results, and also show that in the case of the acyl derivatives substitution occurs mainly in the *p*-position. In the case of the secondary base, as with the primary base, the chief by-product is a *p*-derivative, and an *o*-compound is also produced. The qualitative examination of another secondary base is described on p. 2461.

(4), (5), (6), and (7). The four tertiary bases yielded closely similar results. Benzyldiethylamine has been nitrated by Noelting and Kregczy (*Bull. Soc. chim.*, 1916, **19**, 335) and by Flürscheim and Holmes (this vol., p. 1567), who obtained values varying from 34 to 54% of *m*-isomeride according to the conditions. Most of these experiments, however, refer to nitration in sulphuric acid. Holmes and Ingold examined the nitration product of dibenzylmethylamine and isolated only the *pp'*-dinitro-isomeride in the crystalline condition, but the results now described show that considerable quantities of the *mp'*- or *mm'*-dinitro-compound (probably both) must have been present.

Directive Action of the Ions, the Undissociated Salts, and the Bases.

When an amine is dissolved in water, or in acid solvents, such as concentrated nitric and sulphuric acids, which are good

ionising media but poor electrolytes, the following equilibria obtain,

$$\underset{(ion)}{R_3NH^+} + X^- \rightleftharpoons \underset{(salt)}{R_3NHX} \rightleftharpoons \underset{(base)}{R_3N} + HX,$$

and any effects which are observed (*e.g.*, nuclear substitution) will be the sum of the effects on the three forms implicated. To determine the behaviour of the three forms is the object of experiments such as those described herein, but for this purpose some assistance from theory is required.

The results recorded in Parts IV, V, VI, and VII of this series (this vol., pp. 1305, 1310, 1328, 1684) were interpreted in the light of a hypothesis of electronic strain, the main suppositions underlying which (so far as concerns the case under discussion) may be summarised as follows: (i) Electronic strain, originating in a substituting atom, may be transmitted from carbon atom to carbon atom by two *unidirectional* * processes (*A*) and (*B*),

$$\vec{C}\!-\!\vec{C}\!-\!\vec{C}\!-\!\vec{C}\!-\!C \quad \ldots\ldots\ldots (A)$$

$$\overset{\rightarrow}{}\!\!\overset{\rightarrow}{}\!\!\overset{\rightarrow}{}\!\!\overset{\rightarrow}{}\!\! \quad \ldots\ldots\ldots (B)$$

(*A*) predominating in saturated chains and (*B*) in chains of unsaturated carbon atoms owing to the assumed looser binding of the valency electrons in the double linking. (ii) The *direction* of the effect is prescribed by the principle of resistance to disturbance of the octets, and its *magnitude* by the assumed octet-stability of the substituting atom as deduced from its position in the periodic classification (*e.g.*, proximity to the inert-gas group); naturally the disturbance will diminish with distance from the substituting atom.

In applying these views to the nuclear substitution of bases in acid media, it is necessary to form a picture of the molecular condition of the base. Moore and Winmill have shown (J., 1912, **101**, 1635) that the ammonium hydroxides corresponding with primary, secondary, and tertiary amines exist largely undissociated in aqueous solution, in equilibrium, on the one hand, with varying amounts of the amines and water (which is in large excess), and,

* Alternating strain, or displacement $\vec{C}\!-\!\overset{\leftarrow}{C}\!-\!\vec{C}\!-\!\overset{\leftarrow}{C}\!-\!C$ such as is required by the theory of alternate polarities as usually applied, is regarded as disproved by the comparison of benzylamines and benzyl ethers referred to above, and by the sequences N>O>F and S>O established for *op*-directive power in Parts V, VI, and VII. Also, the nitroamine hypothesis by the aid of which Flürscheim's theory was applied to the nitration of benzylamine derivatives is definitely abandoned by the present authors for reasons shown in this and the following paper.

on the other, with somewhat small proportions of the ammonium and hydroxide ions:

$$NR_3 + H_2O \underset{x}{\rightleftharpoons} NR_3H{\cdot}OH\,* \underset{y}{\rightleftharpoons} NR_3H^+ + OH^-.$$

Partly in order to account for the presence of these large quantities of undissociated hydroxides, and partly to explain the enormous increase of strength which occurs in passing from primary, secondary, or tertiary bases (all of which are weak electrolytes) to quaternary bases, which resemble the hydroxides of the alkali metals, Moore advanced the suggestion (*ibid.*, p. 1673) that in the undissociated primary, secondary, and tertiary hydroxides the hydroxyl group is attached through hydrogen (*Y*). An electronic interpretation of this, based on the theory of co-ordinated hydrogen, would be represented by (*Z*), where the dotted lines *xx* and *yy* indicate the two possible ways in which dissociation can occur to enable the negative hydrogen atom—it has a half-share in four electrons—to recover its neutrality. These two modes of dissociation correspond with the reactions (*x*) and (*y*) in the above equation. Obviously structures (*Y*) and (*Z*) are not applicable to quaternary compounds, which, as strong electrolytes, would be expected to be fully ionised, free dissociation being limited only by the electrostatic attraction of the ions.

(*Y*) $R_3N{-}H{-}OH$ $\qquad$ $R_3\overset{+}{N}\overset{x\ y}{:}H\overset{x\ y}{:}\overset{-}{O}H$ (*Z*)

Now there seems to be no structural reason why this hypothesis concerning ammonium hydroxides dissolved in water should not be applied to the salts dissolved in the corresponding non-aqueous media—the nitrates in nitric acid, the hydrogen sulphates in sulphuric acid, etc. Nitric and sulphuric acids are both feebly conducting, but highly dissociating solvents. The conductivity of quaternary ammonium salts is of a similar order to that of the hydroxides (Noyes, *J. Amer. Chem. Soc.*, 1925, **47**, 3025). In non-aqueous solvents, the dissociation of neutral salts is evidently considerably less than in corresponding aqueous solutions (Kraus, "Properties of Electrolytically Conducting Systems," 1922), and Walden and Centnerszwer's measurements (*Z. physikal. Chem.*, 1902, **39**, 528) indicate the same "jump" in conductivity in passing from salts of primary, secondary, and tertiary bases to salts of quaternary bases, as is observed in aqueous solution in the case of the bases

* If any non-ionising amine-hydrate (NR_3,H_2O) were present, this would be included in the proportions given by Moore and Winmill for NR_3, and would not be confused with the potentially ionising, but actually undissociated, ammonium hydroxide, $NR_3H{\cdot}OH$.

themselves. We therefore adopt the view that in nitric acid solutions of primary, secondary, and tertiary amines the entity (*C*) is present, largely undissociated, but also to some extent dissociated in the two ways represented.* In the case of the quaternary salts, however, we have condition (*D*), in which ionisation is complete, and the separation of the free ions is limited only by electrostriction.

(*C*) $R_3\overset{x\ y}{\overset{+}{N}:\overset{-}{H}:}ONO_2$ $[R_4N]^+ONO_2^-$ (*D*)

It is now possible to determine the behaviour of the three entities present, or potentially present, under the conditions of the nitration of a benzylamine derivative.

(i) *The Ion.*—According to the hypothesis summarised at the commencement of this section the benzylammonium ion (*E*) should substitute largely in the *m*-position,† a conclusion identical with that already advanced by Robinson (*Chem. and Ind.*, 1925, **44**, 1563) and by Flürscheim and Holmes (*loc. cit.*) on rather different grounds. To precisely what *extent* *m*-substitution should occur it is impossible to foretell on a purely theoretical basis, but it does follow that the proportion of *m*-substitution in a perfectly free ion would be greater than is observed for a quaternary salt at finite dilution. Combining this theoretical inference with the results of experiment (p. 2441), we may say that the free benzylammonium ion should be *almost wholly* m-*substituting*.

(ii) *The Salt.*—For similar reasons the undissociated benzylammonium salts must be *largely* m-*substituting*, although less completely so than the ions; for the effect of the dipole ($\beta\gamma$) on the electrons of the carbon atom (α) in (*F*) must be qualitatively similar to, although somewhat smaller than, the corresponding effect of the free positive charge in (*E*).‡ This conclusion does not accord with that derived by Flürscheim (*Chem. and Ind.*, 1926, **45**, 220) and Robinson (*ibid.*, p. 219) from their respective views, but it appears to be consistent with the experimental data,§ and is strongly

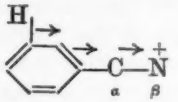
* It has to be remembered that the dissociated portions may never be entirely out of reach of one another's influence. An undissociated salt of type (*D*) should show diminished but still substantial *m*-substitution.

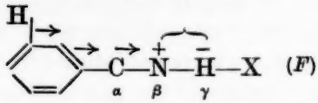
† In confirmation, it has been found that trimethyl-β-phenylethylammonium picrate gives only about 20% of *m*-derivative on nitration in nitric acid.

‡ Thus, if the atomic distances were equal and the charges acted as though concentrated at the centres of the atoms, the attraction of the dipole on the electrons of Cα would be 75% of that of the free positive charge.

§ Flürscheim and Holmes (*loc. cit.*) have provided evidence that *m*-nitration of benzylamine derivatives is diminished by depressing the ionic dissociation, but it does not seem to us to follow from their work that the true salt would substitute wholly *op*-.

supported by analogy with the type $C_6H_5 \cdot CR_2 \cdot NO_2$, the discussion of which is, however, deferred to the following paper.


(*E*)


(*F*)

(iii) *The Base.*—Since, according to the hypothesis summarised, any *m*-substitution in the types $C_6H_5 \cdot CH_2X$, $C_6H_5 \cdot CHX_2$, etc., where X is a *neutral* atom, must be caused by electronic restraint, originating in the firm binding of the electrons in X and transmitted as in (*E*), it follows that the effect must be greatest for fluorine (most stable octet) and least for nitrogen (least stable octet) in the series F>Cl>O>N (compare *Chem. and Ind.*, 1926, **45**, 357). Combining Hove's work on the nitration of benzal fluoride (*Bull. Acad. roy. Belg.*, 1913, **3**, 1082), Swartz's on benzotrifluoride (*ibid.*, 1920, **6**, 389), Holleman's on benzyl-, benzal-, and benzotri-chlorides (*Rec. trav. chim.*, 1914, **33**, 1), Staedel's (*Annalen*, 1883, **217**, 177) and Holmes and Ingold's (*loc. cit.*) on benzyl ethers, and Dr. J. W. Baker's (private communication) on benzal acetals, we obtain the following data:

Nitration of	F	>	Cl	>	O	>	N	
$C_6H_5 \cdot CH_2X$	—		4		0*		—	% *meta*
$C_6H_5 \cdot CHX_2$	65*		35		0*		—	,,
$C_6H_5 \cdot CX_3$	99		64		—		—	,,

* Approximate values.

This verifies the theoretical sequence for F, Cl, and O, and also indicates that free benzylamines, and indeed all completely uncharged benzylamine derivatives, must be *almost wholly* op-*substituting*.

The interpretation of the experimental results on the basis of these generalisations requires little elaboration. The quaternary salt (1) illustrates most closely the directive action of the ion, and the primary, secondary, and tertiary compounds (2—7) that of the undissociated salts. Two views are possible as to the reason for the variation (44—76%) of the *m*-content in these latter cases; either, the lower figure is nearest that proper to the salt,* in which case increases must be ascribed to dissociation at *yy* (formula *C*); or, the upper figure represents most nearly the effect of the salt, diminutions being attributed to dissociation at *xx*. Actually we incline to the former view, since on this assumption the results agree

* That is, the primary salt; the proportions of *m*-substitution appropriate to the secondary and tertiary undissociated salts should be less, owing to electron repulsion by the alkyl groups.

with anticipation based on Moore and Winmill's data for the " real " ionisation constants of primary, secondary, and tertiary aliphatic bases, steric and electrical effects being superposed. In the cases of the acyl derivatives (7—10), dissociation at *xx* also becomes important, however, and this leads to low values for the monoacyl and still lower ones for diacyl derivatives.*

In conclusion, it should be remarked that, in applying the above views to our experiments, we have not lost sight of the fact that Flürscheim's theory, as recently extended by Flürscheim and Holmes (*loc. cit.*), and Robinson's theory are also applicable, although on rather a different basis (ion : *m*- ; salt : *op*-). We propose, however, to defer the discussion of these views to a later paper in which further evidence will be brought to bear on the fundamental question as to whether the undissociated salt exclusively directs *op*-.

Should further investigation confirm the interpretation given, it would be applicable along obvious lines to bases of other types (*e.g.*, aniline and β-phenylethylamine derivatives) and would lead to new interpretations of the anomalies observed in the substitution of bases generally.

At the time of writing, Ing and Robinson's full results on the nitration of benzylamine derivatives are not available, but in a preliminary publication (*Chem. and Ind.*, 1926, **45**, 10) Holmes and Ingold's results were criticised on the grounds that the primary and secondary bases give appreciable quantities of *p*-nitro-derivatives on nitration at 100°, that *mm'*-dinitrodibenzylmethylamine is contained in the nitration product of dibenzylmethylamine, and *p*-nitrodiacetylbenzylamine in that of diacetylbenzylamine. Although the last-mentioned compound is probably not nitrated as such under the conditions employed (see p. 2461), it may at once be agreed that these criticisms are justified inasmuch as the present quantitative investigation accords more closely with the general conclusions of Ing and Robinson than with those of Holmes and Ingold in each of these three particulars (compare pp. 2442, 2456 and 2457).

Experimental.

General.—The ratio of *m*- to *op*-substitution obtaining in the mononitration of the eleven benzylamine derivatives mentioned below was determined by means of Francis and Hill's quantitative bromination process (*loc. cit.*) modified in details. In two of the cases, *viz.*, benzylamine and triethylbenzylammonium hydroxide, the results thus obtained are closely confirmed by the actual separ-

* It is assumed that the nitrogen atom does not acquire a sufficiently strong or permanent charge by betaine isomerisation (Ingold and Ingold, this vol., p. 1311) for any considerable *m*-substitution to arise from this cause.

ation of the isomerides, and in the last-mentioned instance a combination of separation and analysis by the bromination method was employed in order to obtain the final value. The separations are described in the individual cases, but the following remarks regarding the bromination process apply generally.

The modifications introduced into Francis and Hill's method are based partly on those advocated by Kolthoff and Robinson (*Rec. trav. chim.*, 1926, **45**, 169), and partly on our own experience. Potassium bromide–bromate solution and sodium thiosulphate solution were made exactly $N/10$ by standardisation against freshly-distilled aniline. Titanous chloride, prepared in accordance with Francis and Hill's directions, was standardised daily against the other two solutions under the conditions employed in the estimation itself. For the estimation, a quantity (B grams) was dissolved in 25 c.c. of 96% alcohol in a flask fitted with a tube leading to the bottom for the introduction of carbon dioxide, and with a short tube into which the nozzle of the burettes could be inserted; 25 c.c. of 50% sulphuric acid were added, and the mixture heated to boiling whilst a rapid stream of air-free carbon dioxide was passed through. The passage of gas was continued whilst a known volume of standard titanous chloride, containing not less than 0·007 equiv., was run in through the short tube out of contact with air, after which the solution was boiled for 5 minutes and then cooled to 0°. Sufficient ice was then added to maintain the temperature at −4° throughout the remainder of the estimation, and standard bromate solution was run in until a blue colour was given immediately by starch–iodide solution used externally.* The current of carbon dioxide which had been continued up to this stage was then stopped, and a further 3 c.c. of bromate were added (total D c.c.). After a further 5 minutes, during which the reaction proceeded to completion, 0·5 c.c. of saturated potassium iodide solution and 1 c.c. of concentrated starch solution were introduced, and the mixture was made up to 500 c.c. with water and quickly titrated with thiosulphate (E c.c.). The end-point usually consists of a change from blue to yellow or brown, the exact shade depending on the particular derivative under examination. If A represents the number of equivs. of titanous chloride used, and C the molecular weight divided by the number of nitro-groups in the molecule, then F, the bromination number, is given by $F = 3 - C\{A - 0{\cdot}0001\ (D - E)\}/2B$. In the simplest case, the proportion of *m*-isomeride in the mixture examined can be directly calculated from this, but the procedure we employed was a more complex one for the following reasons: Francis and Hill

* After sufficient experience this test can be dispensed with, the changing tint of the solution being an adequate guide.

discuss the various sources of error which may affect the results in certain cases, and mention particularly (*a*) oxidation with destruction of the molecule, (*b*) the precipitation of incompletely brominated products, and (*c*) the replacement by bromine of the directing group. Error (*b*) is overcome by the use of sufficient alcohol, and (*a*) and (*c*) by working at a low temperature, and for each compound there is a temperature below which these disturbances do not enter. In most of the cases which we have investigated, error (*b*) is unimportant under the conditions indicated in the above description, but (*c*) is concerned in varying degrees in the different cases, and in some of them (*a*) appears to enter also. These disturbances are certainly minimised, as Francis and Hill state, by the use of low temperatures, but as the temperatures below which they became inconsiderable were often inconvenient or inaccessible, we have adopted the expedient of working at a uniform temperature, *viz.*, — 4°, which is as low as is consistent with rapid working, under strictly standard conditions, and then deducing the proportion of *m*-isomeride from the bromination number by means of an empirically found relationship between these two quantities, this relationship being determined for each of the cases thus dealt with, by carrying out similar estimations with the pure isomerides and with artificial mixtures of them. The following examples will illustrate the procedure: 0·1538 G. of *mm'*-dinitrodibenzylamine, for which $C=143{\cdot}6$, was reduced with 0·00790 equiv. of titanous chloride; the excess of titanous chloride was removed and the bromination effected by the addition of 84·0 c.c. of *N*/10-bromate–bromide solution; the excess of bromine then required 4·8 c.c. of *N*/10-thiosulphate; hence, $F = 3{\cdot}0093$. From this, by calculation according to Francis and Hill's equations, the *m*-content is 100·9%. Duplicate determinations gave 100·0, 99·1, and 100·0%. In the various isomeric dinitrodibenzylamines, the disturbances (*a*) and (*b*) mentioned above are inappreciable under the conditions used, and this example also illustrates the fact that disturbance (*c*) cannot affect *m*-compounds. It does, however, affect the *p*-compounds in this series to the extent of about 8% on the value of *F* for the *pp'*-dinitro-compound. To illustrate the method of using the empirical relation in such cases, the following example may be given: A mixture containing 53·6% of *mm'*-dinitrodibenzylamine and 46·4% of the *pp'*-isomeride was reduced and brominated, the value $F = 2{\cdot}593$ being obtained. Direct calculation of the *m*-content from this would involve an error of 6%. However, by interpolation from the values of *F* for the two constituents it is found that $F = 2{\cdot}593$ corresponds with a *m*-content of 53%, an error of 0·6% only. It should be added that, since the empirical

relation between F and the m-content has been determined mainly by means of the m- and p-isomerides, there is a tacit assumption, in applying this relation to products of nitration, that any o-compound present will behave like the p-compound. Such experiments as we have done on the estimation of o-nitrobenzylamine derivatives (see pp. 2456 and 2460) show that this is the case, and in any event all the more complete separations of nitration products of benzylamine derivatives which have hitherto been effected agree in showing that the amount of o-substitution is always small. For these reasons, we believe that no serious error is introduced in connexion with the above assumption regarding the behaviour of o-compounds.

The nitration products may be used for these estimations in the form of either the free nitro-bases, or their hydrochlorides or acetyl derivatives, but the use of nitrates or picrates leads to undesirable complications owing to the action of the titanous chloride on the anion. Nitrates were therefore first converted into acetyl derivatives by boiling with acetic anhydride and sodium acetate as described below; and picrates were weighed as such and dissolved in hydrochloric acid, the picric acid being quantitatively extracted by shaking with benzene and the hydrochloric acid solution being taken for the estimation.

(1) *Nitration of Benzyltriethylammonium Picrate.*

Benzyltriethylammonium Picrate.—Benzyltriethylammonium iodide was prepared by the action of ethyl iodide on diethylbenzylamine (Meyer, *Ber.*, 1877, **10**, 310), and converted into the *picrate*, which crystallised from water as yellow prisms, m. p. 124° (Found : C, 54·1; H, 5·8. $C_{19}H_{24}O_7N_4$ requires C, 54·3; H, 5·7%).

m-*Nitrobenzyltriethylammonium Picrate.*—*m*-Nitrobenzyldiethylamine was prepared by the action of diethylamine on *m*-nitrobenzyl chloride (compare Noelting and Kregczy, *Bull. Soc. chim.*, 1916, **19**, 335) and converted into the quaternary iodide, following the method used by Meyer (*loc. cit.*) in the case of the parent substance. The *picrate*, precipitated as in the previous instance, and crystallised from water, formed yellow prisms, m. p. 149° (Found : C, 48·9; H, 4·8. $C_{19}H_{23}O_9N_5$ requires C, 49·0; H, 5·0%).

p-*Nitrobenzyltriethylammonium Picrate.*—This was prepared from *p*-nitrobenzyl chloride *via* *p*-nitrobenzyldiethylamine and the quaternary iodide exactly as in the previous case. It forms yellow prisms, m. p. 155° (Found : C, 48·8; H, 4·9. $C_{19}H_{23}O_9N_5$ requires C, 49·0; H, 5·0%).

Proportion of m-*Substitution.* (a) *By Estimation.*—Benzyltriethylammonium picrate was added in small portions to 7·5 times its weight of nitric acid (d 1·5) kept at − 5°. After an hour, by which

time atmospheric temperature had been attained, ice was added equivalent to 1·5 vols. of water. Gaseous ammonia was then passed in (the temperature meanwhile rising to 70—80°) until the solution was alkaline. The precipitate, which was collected from the cooled solution, consisted of the pure *m*-isomeride; it had m. p. 150° and did not depress the m. p. of the synthesised specimen. The yield was 64·0%. The filtrate from this was evaporated to dryness and extracted repeatedly with hot acetone in which ammonium nitrate is scarcely soluble. The residue from the acetone was then crystallised once from water to remove any trace of ammonium salts if present. The yield was 28·8%, thus leaving 7·2% to be accounted for either as material put out of action by oxidation or as nitro-compounds which could not be separated from the inorganic salts. The 28·8% was obviously a mixture of isomerides. It had m. p. 125—130°, which was raised by admixture with either the *m*- or *p*-compound, and gave correct figures on analysis (Found: C, 48·9; H, 5·2%). It was converted into chloride by means of benzene and hydrochloric acid, and the chloride reduced and brominated as previously described, the value $F = 2·609$ being obtained. Pure *p*-nitrobenzyltriethylammonium picrate, similarly treated, gave $F = 2·149$, and the pure *m*-nitro-compound $F = 3·011$. The rectilinear character of the line connecting F with the *m*-content of mixtures was confirmed by the analysis of mixtures of the *m*- and *p*-isomerides. A mixture containing 32·1% of *m*-compound gave $F = 2·402$, and one containing 73·3% gave $F = 2·803$. From this it follows that $F = 2·609$ corresponds with a *m*-content of 54·5%. This means that $64·0 + 28·8 \times 0·545 = 79·7\%$ of the whole or 86% of the mononitro-compounds isolated (92·8%) is the *m*-derivative. If it be assumed that the composition of the material unisolated is the same as that of the second fraction, the total *m*-content would be 84%; hence we may accept *85%* as an approximation to the true value.

(b) *By Separation.*—Benzyltriethylammonium picrate (10 g.) was added in small quantities to 25 c.c. of 95% nitric acid at 20°. The addition occupied 0·5 hour and the solution was kept for a further hour at the same temperature. Crushed ice (50 g.) was then added, and gaseous ammonia passed into the solution through a fine capillary tube. The temperature rose to 70°, and when the alkaline solution had cooled, the precipitate (10·0 g; 91%) was collected. This had m. p. 140—142°, which was raised by addition of the *m*-compound, and therefore consisted mainly, but not wholly, of this isomeride. One crystallisation from water raised the m. p. to 146°, and a second to 148°; further crystallisations effected no appreciable change. Admixture with the synthesised *m*-compound then

caused no depression of m. p., and admixture with the *p*-isomeride caused a large depression. The specimen, m. p. 148°, may therefore be regarded as practically pure *m*-nitro-compound. The yield was 8·70 g. (79% of theory) which agrees closely with the value obtained in (a), *viz.*, 85%.

(2) *Nitration of Benzylamine.*

(a) *Estimation.*—Several experiments were carried out conforming as closely as possible to the following conditions: The base was run through a capillary tube into ten times its weight of nitric acid (*d* 1·5), contained in a vessel cooled by ice, at just such a rate that no brown fumes were evolved. After 2 hours, the mixture was allowed to warm to the room temperature during another 2 hours, and then mixed with ice. After a further 2 hours the precipitated salt was collected, and the filtrate evaporated to dryness at the ordinary temperature in a high vacuum. The nitrobenzylammonium nitrates thus obtained, m. p. 160—190°, were converted into acetyl derivatives by boiling them with acetic anhydride (40 parts) and sodium acetate (1 part) for 15 minutes; the products were warmed with water to destroy acetic anhydride, basified with potassium hydroxide, and extracted with chloroform. The yields were uniformly 94—95%, the remaining 5—6% probably representing material destroyed or converted into benzoic acid by oxidation. Desiccation for several days in a good vacuum was necessary to remove the last traces of chloroform. The product was quite solid, but always melted over a long range (about 60—100°) [Found: (nitrates) (i) C, 39·0; H, 4·3; (ii) C, 38·9; H, 4·6; (iii) C, 39·6; H, 4·2; (acetyl derivatives) (iv) C, 54·6; H, 5·3; (v) C, 55·5; H, 5·4; (vi) C, 55·1; H, 5·0. Calc.: C, 39·2; H, 4·3 and C, 55·6; H, 5·1%, respectively]. For the establishment of the relation between the bromination number and the *m*-content of mixtures of the isomeric nitro-acetyl derivatives, the three isomeric nitrobenzylamines were prepared and converted into the acetyl derivatives in the way described. The m. p.'s of the *o*-, *m*-, and *p*-hydrochlorides were 248°, *225°*, and *256°* (decomp.); those of the nitrates 174°, *187°*, and *214°* (decomp.); and those of the acetyl derivatives 99°, *107°*, and *133°*, respectively, the italicised numbers being in correction of the m. p.'s recorded by Amsel and Hofmann (*Ber.*, 1886, **19**, 1286), Gabriel and Henders (*Ber.*, 1887, **20**, 2869), Hafner (*Ber.*, 1890, **23**, 330), and Holmes and Ingold (*loc. cit.*). Aceto-*p*-nitrobenzylamide gave $F = 2·674$, and mixtures with the *m*-nitro-isomeride containing 40·0, 47·6, and 53·2% of *m*-compound gave $F = 2·930$, 2·973, and 3·032, respectively, the relationship between these being linear. The following values of F were obtained from the nitration products:

(i) 2·958; (ii) 2·951; (iii) 2·932; (iv) 2·936; (v) 2·982; and (vi) 2·889. These correspond with the following meta-contents: (i) 44%, (ii) 43%, (iii) 40%, (iv) 41%, (v) 48%, (vi) 34%, respectively. Omitting (vi), the mean is *43*%, and the maximum individual variation is 5%. The investigation described below shows that about the same amount of *p*-compound is simultaneously formed, and that the *o*-isomeride is also present.

(b) *Separation.*—The nitrates of *m*- and *p*-nitrobenzylamine tend to crystallise together, and both pure substances and mixtures melt with decomposition. Satisfactory separation by means of this salt, such as was attempted by Holmes and Ingold, cannot be effected, and the fractions they obtained were certainly not pure isomerides. A moderately satisfactory separation can, however, be carried out by the combined use of the picrates and dichromates, the facts utilised being (*a*) that the *m*- and *p*-picrates, which are highly characteristic substances, show little tendency to crystallise together, (*b*) that the *p*-compound is less soluble in water than the *m*-compound, and (*c*) that the *p*-dichromate is more soluble in water than the *m*-dichromate. *Experiment* (*A*). Benzylamine was nitrated under conditions conforming as closely as possible to those specified above; 70·5% of the material isolated (total yield 93·6%) was obtained as precipitated salt (α), and 29·5% as residue (β). These were examined separately. Fraction (α) was crystallised from 25 parts of hot water and the crystallised portion dissolved in water and treated with aqueous sodium picrate, 30·3% of nearly pure *p*-nitrobenzylammonium picrate being obtained, m. p. 191°. This salt on admixture with genuine *p*-salt (m. p. 194°) melted at 192—193°, and on admixture with the *m*-isomeride (m. p. 197°) melted at about 175°. The filtrate from the first crystallisation was also mixed with sodium picrate, and gave 11·7% of quite pure *m*-nitrobenzylammonium picrate, m. p. 197°. Its identity was similarly confirmed by mixed m. p. determinations with genuine specimens of the corresponding *m*- and *p*-picrates. The mother-liquors from both these crystallisations of picrate were combined, strongly acidified with sulphuric acid and extracted with benzene to remove picric acid. After neutralisation with potassium hydroxide, the solution was evaporated and alcohol added to precipitate the bulk of the potassium sulphate. After filtering, the alcohol was removed by evaporation, and to the well-cooled aqueous solution a concentrated solution of potassium dichromate was added. The base isolated from the crystallised *m*-dichromate was dissolved in dilute nitric acid and the neutralised solution treated with aqueous sodium picrate, 9·2% of the pure picrate of the *m*-nitro-compound, m. p. 197°, being obtained. (The reason for thus converting the

m-dichromate into picrate is that the dichromates decompose on heating, and it is therefore difficult to establish their identity.) Fraction (β) was dissolved in water and treated with sodium picrate; the precipitated picrate had m. p. 193—195°, and consisted of the nearly pure *m*-salt (5·1%). The material in the filtrate was converted into dichromate and the dichromate reconverted into picrate; 6·0% of *m*-picrate, m. p. 195—196°, was obtained. The total quantities thus isolated were: *meta*- 32·0%, *para*- 30·3%. The mother-liquors from these crystallisations almost certainly contained further quantities of each of these isomerides together with the ortho-compound, but the presence of the last rendered separation difficult.

Experiment (*B*). In this separation the picrates were employed whenever possible in order to obtain the most complete isolation of para-isomeride, since there is, at present, no other means of estimating accurately the proportion of this substance. Nitration under the conditions described above led to the isolation of 94·4% of the theoretical quantity of nitrobenzylamine nitrate, which was obtained as two fractions, (α) and (β), constituting respectively 70·6% and 29·4% of the total. Fraction (α) was then crystallised from water as before, and the solid and mother-liquors separately converted into picrate. This was crystallised in a series of fractions, which were regulated by changing the solvent according to the substance tending to separate; when the *m*-compound (stout prisms) was being deposited in greater quantity than the *p*-isomeride (long, slender needles), the deposition of the latter could be largely prevented by adding methyl alcohol, whilst when the *p*-compound tended to separate it could be obtained quite free from the *m*-isomeride by boiling off the methyl alcohol and crystallising from water, in which the *p*-salt is only slightly soluble. The following table indicates the progress of the separation:

Fraction α (70·6%).

Filtrate.	Crystallised material.
(1) *meta*-, m. p. 195—196°, 9·6%.	(4) *para*-, m. p. 192—193°, 21·2%.
(2) *meta*-, m. p. 197°, 3·1%.	(5) *para*-, m. p. 192°, 6·9%.
(3) *para*-, m. p. 192°, 5·1%.	(6) *para*-, m. p. 192°, 1·6%.

Mother-liquors now combined:

(7) *para*-, m. p. 190—191°, 3·0%. (8) *meta*-, m. p. 195°, 4·3%.
(9) *para*-, m. p. 191°, 1·8%.

At this stage the separation was rendered difficult by the presence of the ortho-picrate, and the residues were therefore converted into dichromates and back again into picrates as in experiment (*A*):

(10) *para*-, m. p. 190°, 2·5% (from dissolved dichromates).

Fraction (β) was dissolved in water and converted into picrates, the fractions of which were as follows :

(11) *meta*, m. p. 195°, 1·5%. (12) *meta*-, m. p. 193°, 2·1%.
(13) *meta*-, m. p. 193°, 1·5%.
(14) *meta*-, m. p. 196°, 4·8% (from precipitated dichromates).
(15) *meta*-, m. p. 195°, 1·2% (from precipitated dichromates).

The remaining dichromate fractions on reconversion to picrates gave mixtures which could not be satisfactorily separated. Combined yields : *meta*- 28%, *para*- 42% (total 70%). The following experiment shows that practically the whole of the *p*-isomeride had been separated by this treatment. For use in identifying the above fractions m-*nitrobenzylammonium picrate*, stout prisms, m. p. 197° (Found : C, 40·9, H, 2·9. $C_{13}H_{11}O_9N_5$ requires C, 40·9; H, 2·9%), and p-*nitrobenzylammonium picrate*, slender needles, m. p. 194° (Found : C, 41·1; H, 3·0%), were prepared from the corresponding nitrobenzyl chlorides.

(c) *Oxidation of Unseparated Portion.*—The unseparated portion in the above experiment was converted into free bases and oxidised by adding slightly more than the theoretical quantity of 5% potassium permanganate solution to its boiling suspension in 600 parts of water, the addition being timed to keep pace with decolorisation. After 20 hours' boiling the oxides of manganese were filtered off, and treated with steam in the usual way, and the combined filtrates evaporated, acidified and extracted three times with ether. By drying with sodium sulphate and evaporating, a mixture of nitrobenzoic acids (free from benzoic acid) was obtained as a dry, almost white powder, m. p. 105—110° (Found : C, 50·2; H, 2·9. Calc. : C, 50·3; H, 3·0%) (yield 67%). This was completely soluble in 60 parts of cold chloroform, thereby showing that it could not contain as much as 6% of *p*-nitrobenzoic acid. The barium salt was then prepared and crystallised twice from 35 times its weight of water, and the acid regenerated. In this way, *m*-nitrobenzoic acid, m. p. 136—139°, was obtained, the mixed m. p. with a genuine specimen being 139—140°. The yield was 54% of the original mixed acids; correcting for the solubility of the barium salt in the water used, the proportion of meta- in the mixture becomes 69%. The filtrate from the first crystallisation of the *m*-salt was worked up for acids by means of ether. The acids isolated amounted to 37% of the mixture and contained, by calculation, 8% meta-, 0—6% para-, and 29—23% ortho-. The m. p. was 119—128° and, on admixture with *o*-nitrobenzoic acid, 139—144°; after crystallisation from 20 parts of chloroform 19% of almost pure *o*-nitrobenzoic acid, m. p. 142—145° (mixed m. p. 145—147°), was isolated. Correcting for the solubility of *o*-nitrobenzoic acid in chloroform, 27% of the

original mixture is accounted for as *o*-nitrobenzoic acid. An experiment with a mixture of the *m*- and *p*-compounds having indicated that the oxidation is not seriously selective, the following estimate of the proportions of the isomerides may be given:

	Ortho-.	Meta-.	Para-.
By separation	0%	28%	42%
Oxidation of residues	8	21	1
Total	8	49	43

The nitration of benzylamine was also carried out at 100° as described by Holmes and Ingold (*loc. cit.*), and since the product contained some impurity which rendered the bromination process inapplicable and also interfered with the picrate separation, the whole product was oxidised to a mixture of acids, which did not, however, consist wholly of mononitrobenzoic acids, but which gave 16% of moderately pure *p*-nitrobenzoic acid on separation. Almost all the remaining material gave a sparingly soluble barium salt from which, however, impure *m*-nitrobenzoic acid, m. p. 115—120°, was recovered.

(3) *Nitration of Dibenzylamine.*

Several nitrations were carried out, adhering as closely as possible to the conditions specified in the nitration of benzylamine (p. 2452). The total yields of nitrates were always close to 97% and the product melted at 205—210° (decomp.). The nitrates were converted into the free bases by extraction with chloroform in the presence of potassium hydroxide, and the *m*-content of the bases was determined by the bromination method [Found: (bases) (i) C, 58·2; H, 4·4; (ii) C, 58·1; H, 4·4; (nitrates) (iii) C, 47·8; H 4·1; (iv) C, 48·6; H, 3·8; (v) C, 48·2; H, 3·7. Calc.: C, 58·7; H, 4·2% and C, 48·2; H, 3·7%, respectively].

To establish the relation between the bromination number and the *m*-content of mixtures, *mm'*-dinitrodibenzylamine (m. p. 83°), and *pp'*-dinitrodibenzylamine (m. p. 93°) and mixtures of these containing 53·6% and 66·3% of the former were submitted to analysis in the manner described above; the following results were obtained for the four cases in the order named: $F = 3{\cdot}000$, 2·153, 2·593, 2·727. This establishes a straight line relation. An approximate determination made with a rather small quantity of *oo'*-dinitrodibenzylamine gave $F = 2{\cdot}110$, in fair agreement with the value for the *pp'*-compound.

Analysis of the nitration products yielded the following values of F: (i) 2·797; (ii) 2·785; (iii) 2·884; (iv) 2·794; (v) 2·682; which correspond respectively with the following *mm'*-contents: (i) 76%; (ii) 75%; (iii) 87%; (iv) 76%; (v) 68%. The mean of all these is

76%, and the mean of the three closely-agreeing results (i), (ii), and (iv) is the same. The maximal variation (experiment iii) amounts to 11%.

The base was also nitrated at 100° and the product oxidised; 16% of nearly pure *p*-nitrobenzoic acid (m. p. 230—234°) and 41% of nearly pure *m*-acid (m. p. 125—131°) were isolated (18% unseparated).

(4) *Nitration of Tribenzylamine.*

Tribenzylamine hydrochloride was prepared by Matter's method (D.R.-P., 1917, 301450, compare Friedländer, 1916—1921, **13**, 247), and the free base liberated and crystallised from methyl alcohol (m. p. 92·5°).

pp'p''-Trinitrotribenzylamine was prepared by a modification of Strakosch's method (*Ber.*, 1873, **6**, 1056). *p*-Nitrobenzyl chloride (10 g.) and ammonia (30 c.c.; *d* 0·880) were heated in a closed tube for 4 hours at 100°, and the resulting brown paste boiled with 10% hydrochloric acid. The suspension thus obtained was extracted with benzene without filtering, and the crystals formed on concentrating the benzene solution were crystallised from ethyl acetate. The nitro-base had m. p. 168° (Found: C, 59·4; H, 4·3. Calc.: C, 59·7; H, 4·3%).

mm'm''-*Trinitrotribenzylamine* was prepared similarly from *m*-nitrobenzyl chloride, the contents of the tube being extracted with methyl alcohol, in which the required base is insoluble. It separated from ethyl acetate in colourless needles, m. p. 163° (Found: C, 59·9; H, 4·4. $C_{21}H_{18}O_6N_4$ requires C, 59·7; H, 4·3%).

Tribenzylamine has been nitrated by Marquardt (*Ber.*, 1886, **19**, 1030) but the products were not definitely identified. The base was nitrated as in the preceding cases, but instead of being worked up for nitrates the mixture was basified and extracted with chloroform. The product was thus obtained as a stiff gum, and the removal of the last traces of chloroform necessitated heating at 100° at a pressure below 1 mm. [Found: (i) C, 59·9; H, 4·0; (ii) C, 59·7; H, 4·4%].

Bromination of the synthetic *p*- and *m*-nitro-compounds gave $F = 2·120$ and 2·638 respectively, and a mixture containing 58·2% of the *m*-isomeride gave $F = 2·403$, indicating the linear relation.

Nitration product (i), yield 74%, gave $F = 2·433$, which corresponds with 60% *m*-substitution. Product (ii), yield 100%, gave $F = 2·394$, which is equivalent to *53%* *m*-substitution. The latter result is regarded as the more trustworthy.

(5) *Nitration of Dibenzylmethylamine.*

Benzyl chloride (20 g.), ethyl alcohol (200 c.c.) and 33% aqueous methylamine (40 c.c.) were mixed and kept for 1 hour at the ordinary

temperature, and then heated to 60° in a closed vessel to complete the reaction. The alcohol was evaporated, sodium hydroxide added, and the mixed bases extracted with ether and distilled. A first fraction, b. p. about 60°/1 mm., consisting essentially of benzylmethylamine was obtained, the bulk of the dibenzylmethylamine distilling at 143°/1 mm.

The base was allowed to flow into 10 parts of nitric acid (*d* 1·5) at 0° as described in case (2), the basic nitration product, which was only partly solid, being isolated as in case (4). Prolonged exposure in a mercury-pump vacuum was necessary to eliminate the last traces of chloroform [Found: (i) C, 60·6; H, 4·9; (ii) C, 59·8; H, 5·4. Calc.: C, 60·0; H, 5·0%].

For the determination of the relation between *m*-content and the bromination number, *mm'*-dinitrodibenzylmethylamine, *pp'*-dinitrodibenzylmethylamine, and mixtures of these containing 40·3% and 72·1% of the *mm'*-isomeride were employed, the corresponding values of *F* being 2·334, 3·022, 2·566, and 2·832, respectively. The relationship is linear. The nitration products gave (i) $F = 2·697$, (ii) $F = 2·776$, which correspond with meta-contents (i) 52%, (ii) 64%. Mean: *58*%.

(6) *Nitration of Benzyldimethylamine.*

This base was prepared as described by Sommelet and Guioth (*Compt. rend.*, 1922, **174**, 687), and was nitrated exactly as in the preceding instance, the product, which was an oil, being isolated with the aid of chloroform as described above. The yield was 89—90% of the theoretical, and it is possible that the bases evaporate slightly during the removal of the chloroform [Found: (i) C, 60·7; H, 6·4; (ii) C, 60·7; H, 6·5; (iii) C, 60·2; H, 6·3. Calc.: C, 60·0; H, 6·7%].

m-*Nitrobenzyldimethylamine.*—Hexamethylenetetramine (15 g.) was dissolved in the smallest possible quantity of boiling alcohol, and a hot alcoholic solution of *m*-nitrobenzyl chloride added. The quaternary salt which separated on cooling was collected, dissolved in the minimal quantity of hot water and heated with 100 c.c. of absolute formic acid for 16 hours on the steam-bath. The evolution of carbon dioxide having ceased, the solution was made alkaline and extracted with ether, and the base remaining after removal of the ether purified by distillation. It was thus obtained as a clear, pale yellow oil, b. p. about 195°/18 mm. (Found: C, 59·8; H, 6·6. $C_9H_{12}O_2N_2$ requires C, 60·0; H, 6·7%).

p-Nitrobenzyldimethylamine has previously been prepared by Friedländer and Mosczyc (*Ber.*, 1895, **28**, 1141) who, however, record neither the b. p. nor any analytical data. We prepared it from

p-nitrobenzyl chloride by the method used for the *m*-isomeride, and obtained a yellow oil, b. p. 146—148°/18 mm. (Found: C, 60·3 H, 6·7. Calc.: C, 60·0; H, 6·7%). The large difference of b. p. between these *m*- and *p*-nitro-compounds is very remarkable, and somewhat similar disparities were observed by Noelting and Kregczy (*loc. cit.*) in the b. p.'s of the homologous *o*-, *m*-, and *p*-nitrobenzyldiethylamines.

To determine the relationship between *m*-content and the bromination number, the above *p*- and *m*-nitro-bases, and artificial mixtures of them containing 55·9% and 57·6% of the *m*-derivative, were analysed under the usual conditions. The results obtained were $F = 2{\cdot}169$, 3·186, 2·717, and 2·750, respectively, which established the linear relation.

Bromination of the nitration products of benzyldimethylamine gave $F =$ (i) 2·752; (ii) 2·741; (iii) 2·776, which correspond with the following proportions of the *m*-isomeride: (i) 58%; (ii) 57%; (iii) 60%. Mean: ***58***%.

(7) *Nitration of Benzyldiethylamine.*

This base has been nitrated by Noelting and Kregczy (*loc. cit.* and by Flürscheim and Holmes (*loc. cit.*) who obtained for the proportion of *m*-isomeride values ranging from 34—54% according to the conditions. Under the conditions employed for the other tertiary bases, we obtained a nitration product (Found: C, 63·1; H, 7·6. Calc.: C, 63·4; H, 7·7%) which gave $F = 2{\cdot}749$ on bromination. The synthesised *p*- and *m*-derivatives gave $F = 2{\cdot}110$ and 3·046, respectively, and mixtures containing 69·8, 51·4 and 32·7% of the *m*-isomeride gave $F = 2{\cdot}933$, 2·694, and 2·549, respectively, from which it follows that the nitration product contained ***51***% of *m*-isomeride.

(8) *Nitration of Acetobenzylamide.*

Acetobenzylamide, prepared by Amsel and Hofmann's method (*loc. cit.*), had b. p. 150°/1 mm. and m. p. 133° (A. and H. give m. p. 125°). It was nitrated and the product isolated with the aid of chloroform as described in case (4). After removal of the chloroform in a vacuum, the residue solidified, but the solid softened and melted indefinitely between about 50° and 100°. Two experiments were performed [Found: (i) C, 55·4; H, 4·8; (ii) C, 55·2; H, 5·0. Calc.: C, 55·6; H, 5·1%]. On bromination these gave respectively $F = 2{\cdot}711$ and 2·729. From the known relation between F and the *m*-content (case 2), these values correspond with (i) 6%, (ii) 8% of meta-isomeride. The mean of these is 7% ***meta-***. The main constituent is para- (Holmes and Ingold, *loc. cit.*).

(9) *Nitration of Acetobenzylmethylamide.*

This amide was prepared as described by Holmes and Ingold (*loc. cit.*); it had b. p. 143°/1 mm. Nitration was effected as in the preceding case, and the product, m. p. 45—65°, isolated by means of chloroform in the same way (Found: C, 57·7; H, 5·8. Calc.: C, 57·7; H, 5·8%). Bromination by the usual method gave $F = 2·707$.

Aceto-*m*- and *p*-nitrobenzylmethylamides were prepared as described by Holmes and Ingold (*loc. cit.*). The m. p. of the *p*-compound was raised to 83° (previously recorded, 81°). Bromination of the *p*-compound and of mixtures of this with the *m*-isomeride containing 49·1% and 54·1% of the latter gave $F = 2·653$, 2·962, and 2·994, respectively; the value of F obtained for the nitration product therefore corresponds with *8% meta-*. The main constituent is para- (*loc. cit.*).

(10) *Nitration of Acetodibenzylamide.*

Dibenzylamine hydrochloride was boiled with acetic anhydride and sodium acetate, and after treatment with water and an excess of sodium hydroxide, the amide was isolated by extraction with ether and distilled, b. p. 194—195°/3 mm. Nitration was effected as in the preceding case and the product, m. p. 135—155°, isolated as usual [Found: (i) C, 58·6; H, 4·6; (ii) C, 58·3; H, 4·3. Calc.: C, 58·4; H, 4·5%].

Aceto-*oo'*-, *mm'*-, and *pp'*-dinitrodibenzylamides were prepared as described by Holmes and Ingold. The m. p. of the *p*-compound was raised to 185° (previously recorded, 183—184°). On bromination, the *oo'*-compound gave $F = 2·227$, the *mm'*-compound $F = 2·850$, and the *pp'*-compound $F = 2·252$; a mixture of the *mm'*- and *pp'*-isomerides containing 61·5% of the former gave $F = 2·614$.

The nitration products on bromination gave the following numbers: (i) $F = 2·386$; (ii) $F = 2·407$, which correspond respectively with 23% and 26% of *m*-compound. The mean may be taken as *25% meta-*. The main nitration product is para-, and ortho- is also formed.

(11) *Nitration of Succinbenzylimide.*

Succinbenzylimide was prepared as described by Werner (J., 1889, **55**, 629), who recorded m. p. 98—99°. Our product, after careful purification for the nitration experiment, had m. p. 103°. Succin-*p*-nitrobenzylimide was similarly prepared by the method of Hoogewerff and van Dorp (*Rec. trav. chim.*, 1899, **18**, 362), who gave m. p. 150—152°; our specimen melted at 153°.

The nitration of succinbenzylimide was carried out just as in the

preceding case except that during the addition of the imide to the nitric acid, and afterwards until ice was added, the temperature of the acid was maintained at or near — 12°. The precipitated nitration product had m. p. about 120°, and amounted to 78% of the theoretical quantity. A further 8% of neutral material, m. p. 110—115°, was obtained by extraction with ether, so that about 14% was hydrolysed or oxidised under the conditions used. The combined fractions were crystallised once from alcohol, and the product from the mother-liquors again crystallised from the same solvent; in this way 64% of the total was obtained as the practically pure *p*-isomeride, m. p. 151—152° (unaltered by admixture with the synthetic specimen). The remaining 36% had m. p. about 90° (Found: C, 55·6; H, 4·0. Calc.: C, 56·4; H, 4·3%), and was analysed by the bromination method. The bromination number was 2·332, whereas that of the pure *p*-isomeride was 2·313, which represents 3% of the *m*-isomeride. Since this applied to only 36% of the total, the corresponding value for the whole product is *1% meta-*. The above separation shows that the main product is para-.

Diacetylbenzylamine.—Various attempts were made to nitrate this substance, using the methods employed in the previous cases and those of Holmes and Ingold, but the results were erratic, varying mixtures of the *m*- and *p*-compounds being obtained. Also the analytical data were unsatisfactory, and it was ascertained that acetic acid is formed in the reaction, evidently by the destruction of the acylamino-grouping. It was therefore decided to change the reagent. A solution of the benzylamine (5 g.) in acetic anhydride (20 g.) was allowed to flow into a solution of nitric acid (1·8 g.; *d* 1·5) in acetic anhydride (8 g.) at — 14°. The mixture was kept below — 10° for 1 hour, and then evaporated in the cold in a good vacuum over potassium hydroxide (Found: C, 57·5; H, 4·8; N, 11·0. Calc.: C, 55·9; H, 5·1; N, 11·9%). These numbers indicate the presence of considerable amounts of impurity, but an approximate analysis by the bromination method showed the *m*-content to be small, and hydrolysis to the nitrobenzylamines indicated the main constituent to be the *p*-isomeride.

Benzylmethylamine.—The application of the bromination method to the nitration product of this substance was found to be affected by disturbances (probably elimination of the side chain) which rendered it impracticable, and the nitration product (conditions as for benzylamine) was therefore oxidised as described on p. 2455. The nitrobenzoic acids contained no benzoic acid (yield 78%) (Found: C, 50·0; H, 3·2%), and on separation by first washing with chloroform and then crystallising the barium salts of the soluble acids,

gave 21% of *p*-nitrobenzoic acid (m. p. 234°) and 61% of *m*-nitrobenzoic acid (m. p. 131—138°), 18% being unseparated; from the solubilities it is estimated that this portion contained 8% of *m*-acid and 4% of *p*-acid. Nitration at 100° followed by similar treatment gave acids, not consisting wholly of mononitrobenzoic acids, which yielded 9% of nearly pure *p*-nitrobenzoic acid on separation by the use of chloroform.

Dibenzyldimethylammonium Picrate.—Dibenzylamine hydrochloride (15 g.) was added to a mixture of methyl iodide (30 g.), alcohol (10 c.c.) and dilute sodium hydroxide (20 c.c.). After keeping for 1 hour, the mixture was heated for 15 minutes on the steam-bath and poured into water. The iodide was collected (m. p. 193°) and converted into picrate, which was recrystallised from water; yellow prisms, m. p. 146° (Found: C, 57·9; H, 4·9. $C_{22}H_{23}O_7N_4$ requires C, 58·2; H, 4·8%).

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CCCXXV.—*The Nature of the Alternating Effect in Carbon Chains. Part IX. The Directive Influence of Groups of the Form* $-CRR'\cdot NO_2$ *in Aromatic Substitution.*

By JOHN WILLIAM BAKER and CHRISTOPHER KELK INGOLD.

As the result of a quantitative study of the nitration of eleven benzylamine derivatives, Goss, Ingold, and Wilson recently concluded (see preceding paper)

(i) that benzylammonium ions substitute very largely in the meta-position (more than 85% for the benzyltriethylammonium ion);

(ii) that undissociated salts also give large proportions of meta-derivatives (less than the ions, however); and

(iii) that the free amines do not yield appreciable amounts of meta-compounds, but on the contrary, give *op*-products.

These inferences were based on a hypothesis of electronic strain transmission (Ingold and Ingold, this vol., p. 1310) and conclusion (i) was regarded as definitely proved by experiment; conclusions (ii) and (iii), however, although affording a completely satisfactory

explanation of the experimental data, could not be considered to be established in the same final manner. Further evidence on these two points was therefore required, and in this paper independent evidence is brought to bear on conclusion (ii), which is of particular importance from the point of view of these memoirs, since it distinguishes the theoretical views advanced therein from those advocated by Robinson and Flürscheim, according to whom (*Chem. and Ind.*, 1926, **45**, 219, 220) undissociated benzylamine salts should substitute ortho- and para-.

The basis of conclusion (ii) was that the action of the dipole contained in the salt-grouping in setting up electronic strain in the relatively rigid systems imagined by Goss, Ingold, and Wilson, must be qualitatively similar to, and not very much smaller than, that of the free charge in the corresponding ion. The difficulty of establishing the point by direct experiment with benzylamine compounds lies, however, in the fact that the dipole arrangement in benzylamine salts is unstable, and that two modes of disruption (into ion and base) give rise to disturbances the extent of which cannot be exactly foretold. We therefore decided to investigate a series of substances analogous to benzylamine salts, but containing a *stable* dipole, and for this purpose selected phenylnitromethane derivatives, in which the salt-like dipole grouping is kept from dissociation by inclusion in a semipolar double-bonded arrangement (Sugden, Read, and Wilkins, J., 1925, **127**, 1525). Should our conclusions be correct, it is to be expected that phenylnitromethane derivatives would, in general, give considerable proportions of meta-derivatives, and that phenylnitromethane itself (II) would nitrate in the *m*-position to approximately the same extent (44—49%) as benzylamine, which Goss, Ingold, and Wilson assumed to substitute mainly through the undissociated salt (I) (*loc. cit.*). In verification of this prediction we have found that phenylnitromethane yields 48—50% of the *m*-nitro-derivative.

$PhCH_2\cdot\overset{+}{N}H_2-\overset{-}{H}X$ (I; meta-, 44—49%.) $PhCH_2\cdot\overset{+}{N}O-\overset{-}{O}$ (II; meta-, 48—50%.)

In spite of this very close agreement we deemed it essential to supplement the result by studying a series of derivatives of phenylnitromethane—for reasons which can be explained only by reference to the history of phenylnitromethane substitutions.

The nitration of phenylnitromethane itself was first carried out by Holleman (*Rec. trav. chim.*, 1895, **14**, 123) who obtained the *m*-nitro-derivative, which, he stated, constituted the bulk of the nitration product. When summarising the previous literature on directive action in aromatic substitution, Flürscheim, in 1902 (*J.*

pr. Chem., **66**, 328), referred to Holleman's observation as the only recorded instance of orientation in a direction which appeared to be contrary to the requirements of his theory. Since, according to that theory, the nitro-group is bound to carbon more feebly than is hydrogen (compare the explanation given for the meta-directive action of the nitro-group in nitrobenzene), the group $-CH_2 \cdot NO_2$ should be more strongly bound to the benzene ring than the group $-CH_3$; that is to say, the nitromethyl group in phenylnitromethane should direct ortho-para- (III) even more strongly than does the methyl group in toluene. Toluene gives 3% of *m*-nitrotoluene, and consequently phenylnitromethane should give definitely less than 3% of the *m*-derivative. Therefore, to account for Holleman's result Flürscheim advanced the suggestion that phenylnitromethane substitutes through an *aci*-form (IV) containing unsaturated tervalent nitrogen:

$C_6H_5—CH_2—NO_2$ (III; *op*-substituting.)

$C_6H_5—CH(O)—N \cdot OH$ (IV; *m*-substituting.)

It is evident, however, that this could not occur in the case of a tertiary nitro-compound, $C_6H_5 \cdot CR_2 \cdot NO_2$, and, to establish his mechanism, Flürscheim investigated the nitration of phenylbromocyanonitromethane (V). In this case he observed (*loc. cit.*) the exclusive *op*-substitution demanded by his theory, a detailed search failing to reveal the presence of any trace of *m*-compound.

We were led to re-examine this case, first, because the suggested analogy with benzylamine salts, which distinguishes our view from Robinson's, remains valid only provided that phenylnitromethane substitutes through its ordinary form (III), and not through the *aci*-form (IV); secondly, because Flürscheim's theory of aromatic substitution, both in its original and present forms (Flürscheim and Holmes, this vol., p. 1562) is fundamentally dependent on the correctness of the explanation he has given for the substitution of phenylnitromethane; and, thirdly, because the exclusive *op*-substitution of phenylbromocyanonitromethane claimed by Flürscheim is unequivocally contrary to, and would, if true, overthrow, our own view as developed in the preceding parts of this series.

Regarding the first point, it seemed to us highly improbable, despite the apparently convincing character of Flürscheim's experimental demonstration, that phenylnitromethane should substitute in an *acid* medium through an *aci*-form such as (IV). Even if this form be present, the proportion must be excessively small, and therefore in order to account for the predominating *m*-substitution it has to be assumed that the velocity of *m*-nitration of (IV) is so

much greater than the velocity of *op*-nitration of (III) that the large disparity in the active masses is counterbalanced. This is entirely contrary to general experience, according to which *op*-directed substitutions have the greater velocity (compare Ingold and Ingold, this vol., p. 1313). To render the matter certain, however, we have repeated the nitration of phenylbromocyanonitromethane (V) with the same reagent and at the same temperature as used by Flürscheim, and have found that, contrary to his statement, relatively little of the *p*-isomeride is produced and that more than 50% of the product consists of the *m*-nitro-derivative. This shows conclusively that phenylnitromethanes nitrate through their ordinary forms, as the analogy with benzylamine salts requires; it also confirms our view that the undissociated benzylamine salts are largely *m*-substituting, against the contrary views of Robinson and Flürscheim.

(V.) $C_6H_5—C(CN)(NO_2)Br$ $C_6H_5—C(CH_3)(NO_2)CH_3$ (VI.)

Although significant and historically interesting, since, had the original experimental work been correctly performed, Flürscheim's theory, outlined in the same paper, could scarcely have been advanced, the case of phenylbromocyanonitromethane is not the most crucial one that can be devised in order to test that theory; for the bromine atom *might* be assumed, improbable as it may appear, to give rise to the condition $C_6H_5—C(Br)$, leading to *m*-substitution, despite the contrary action of the nitro- and cyano-groups.* We have therefore also investigated the nitration of β-phenyl-β-nitropropane (VI). According to Flürscheim's theory, the methyl group has an intrinsic affinity demand approximately *equal* to that of hydrogen, and, when joined to a saturated atom, cannot form a bond of greater affinity content (*J. pr. Chem.*, 1907, **76**, 197; *Chem. and Ind.*, 1925, **44**, 249, 563). Therefore it follows from this theory (but not from ours, see below) that the methyl groups in phenylnitropropane will offer no disturbance, and, since the nitro-group is tertiary, the side-chain must necessarily direct practically wholly ortho-para. In direct opposition to this hypothesis, we find that about 30% of the *m*-nitro-derivative is formed. This result seems absolutely contrary to Flürscheim's theory, both in its original form and in all the extended forms in which it has

* This appears to be the only possible alternative, since it is admitted that the polar and steric factors ("*p*" and "*s*") are negligible in this case (Flürscheim and Holmes, *ibid.*, p. 1563).

been advanced up to the present—excepting in so far as our own view is admittedly an extension, based partly on that theory.

(VII.) $C_6H_5\cdot C(CH_3)(NO_2)Br$ $C_6H_5\cdot C(Br)(NO_2)Br$ (VIII.)

It remains to be added that, although the electronic-strain hypothesis appears to afford a very satisfactory explanation of the proportions of the isomerides obtained in these cases, two other instances were studied in order to test its applicability more thoroughly. These were phenylbromonitroethane (VII) and phenyldibromonitromethane (VIII). The methyl group attached to saturated carbon is an electron-source (Holmes and Ingold, this vol., p. 1305), and, as such, must oppose *m*-substitution. An illustration of this type of action by methyl is provided by the nitration of methyl and ethyl benzoates (Holleman, *Rec. trav. chim.*, 1899, **18**, 267; *Z. physikal. Chem.*, 1899, **31**, 79; the nitration of other esters of benzoic acid is being investigated):

$C_6H_5\cdot CO_2\cdot CH_2\text{—}H$ (meta-, 73%.) $C_6H_5\cdot CO_2\cdot CH_2 \leftarrow CH_3$ (meta-, 68%.)

The bromine atom, analogously situated, attracts electrons, and therefore must promote *m*-substitution, the action being similar to, but less powerful than (*Chem. and Ind.*, 1926, **45**, 357), that of chlorine (Holleman, *Rec. trav. chim.*, 1914, **33**, 1):

$C_6H_5\cdot CH_2 \rightarrow Cl$ (meta-, 4·2%.) $C_6H_5\cdot CH \rightrightarrows Cl_2$ (meta-, 34%.) $C_6H_5\cdot C \equiv Cl_3$ (meta-, 65%.)

The influence of a single similarly placed cyano-group which contains within itself the elements of both these opposing effects would probably be small. Thus we have the following theoretical sequence of groups arranged in order of their *m*-directive power:

Theoretical Order:

—(increasing meta-)→

$-C(CH_3)(CH_3)\rightarrow NO_2$, $-C(CH_3)(Br)\rightarrow NO_2$, $[-C(H)(H)\rightarrow NO_2]$*, $-C(CN)(Br)\rightarrow NO_2$, $-C(Br)(Br)\rightarrow NO_2$

Found (% meta-):

(29) (40) (48) * (52) (84)

* Compare benzylamine salt.

The figures recorded in the lower line represent the approximate proportions of meta-isomeride observed for each case and serve to show how closely the theoretical requirements are fulfilled.

EXPERIMENTAL.

(A) *Preparation of Phenylnitromethane Derivatives.*

1. *Phenylnitromethane*, $CH_2Ph{\cdot}NO_2$.—This was prepared by Holleman's method (*Rec. trav. chim.*, 1894, **13**, 405) from benzyl chloride and silver nitrite. The product had b. p. 110°/8 mm. (Found: C, 61·3; H, 5·3. Calc.: C, 61·2; H, 5·1%).

2. *Phenylbromocyanonitromethane*, $CPhBr(CN){\cdot}NO_2$.—The sodium salt of *aci*-phenylcyanonitromethane was prepared by Wislicenus and Ender's method (*Ber.*, 1902, **35**, 1757) and carefully purified by crystallisation from absolute alcohol. The pure salt was converted into phenylbromocyanonitromethane by Flürscheim's method (*loc. cit.*) [Found: (Sample A) C, 40·2; H, 2·3; (Sample B) C, 40·4; H, 2·3. Calc.: C, 39·8; H, 2·1%].

3. *β-Phenyl-β-nitropropane*, $CMe_2Ph{\cdot}NO_2$.—This was prepared by side-chain nitration of *iso*propylbenzene (compare Konovalov, *Ber.*, 1895, **28**, 1856) under the following conditions. *iso*Propylbenzene (32 c.c.) was boiled under reflux for 10 hours with 250 c.c. of dilute nitric acid (*d* 1·075), and the cooled mixture made strongly alkaline with potassium hydroxide and extracted with ether. The residue from the ether was fractionally distilled, a large amount of unchanged hydrocarbon being recovered and used again, and a small fraction of the nitro-compound, b. p. 120—140°/15 mm., obtained. After many repetitions of this experiment the fractions of nitro-compound were combined and redistilled repeatedly until a fraction, b. p. 123—128°/12 mm., was obtained. Benzoic acid is also formed in this experiment, and the loss of material through this cause was greatly increased when it was attempted to secure a greater degree of nitration in one operation [Found: (Sample A) C, 65·5; H, 6·6; (Sample B) C, 65·2; H, 6·3. Calc.: C, 65·5; H, 6·7%].

4. *α-Phenyl-α-bromo-α-nitroethane*, $CMePhBr{\cdot}NO_2$.—α-Phenyl-α-nitroethane was first prepared by side-chain nitration of ethylbenzene. Konovalov states (*J. Russ. Chem. Soc.*, 1893, **25**, 527; compare *Chem. Zentr.*, 1894, I, 465) that this reaction takes place when 4 c.c. of ethylbenzene are heated with 25 c.c. of nitric acid (*d* 1·075) at 107° in a sealed tube for 5—6 hours, but under these conditions we found it difficult to avoid almost complete oxidation to benzoic acid. Better results were obtained by carrying out a series of partial nitrations as described for phenylnitropropane, except that the mixture, instead of being made strongly alkaline before extraction with ether, was in this case exactly neutralised with sodium carbonate. The nitro-hydrocarbon, which had b. p. 135°/25 mm., was treated in concentrated alcoholic solution with alcoholic sodium ethoxide, and the sodio-derivative collected,

washed with alcohol and ether, and dried on porous porcelain. It was then decomposed in aqueous solution with the theoretical amount of bromine, α-phenyl-α-bromo-α-nitroethane being then precipitated as a pale yellow oil. As this substance decomposed on distillation, it was extracted with pure ether and the last traces of ether were removed in a good vacuum (Found: C, 41·8; H, 3·7. Calc.: C, 41·7; H, 3·5%).

5. *Phenyldibromonitromethane*, $CPhBr_2 \cdot NO_2$.—This was prepared by Ponzio's method (*Gazzetta*, 1908, **38**, ii, 418) from phenylnitromethane [Found: (Sample A) C, 29·8; H, 1·9; (Sample B) C, 29·6; H, 2·1. Calc.: C, 28·5; H, 1·7%].

(B) *Nitration of Phenylnitromethanes and Determination of the Proportion of* m-*Isomeride: General Procedure.*

(Details peculiar to the procedure in individual cases are given in Section C.)

Nitration of Phenylnitromethanes.—The phenylnitromethane derivative was delivered slowly from a dropping-funnel the constricted end of which dipped under the surface of about 8 parts of fuming nitric acid (*d* 1·49) maintained at a known temperature. The addition usually occupied 2—4 hours and the mixture was then kept at the same temperature for a further period. The temperature, the period of addition, and the time for which the mixture was kept after the addition was finished were varied slightly from case to case according to the conditions required to effect complete nitration and to avoid an undue amount of oxidation. The reaction mixture was then poured on ice, basified with sodium hydroxide below 10° (except in the case of phenylnitromethane—see Section C), and the precipitated nitro-compound extracted with ether. The extract was dried with sodium sulphate, and the residue obtained after removal of the ether desiccated in a good vacuum. The aqueous mother-liquors were acidified with hydrochloric acid and the acid fraction recovered and weighed in order to determine the proportion of the phenylnitromethane which had become oxidised.

Oxidation of the Nitration Product to Nitrobenzoic Acids.—The oxidation of the nitration products to mixtures of *o*-, *m*-, and *p*-nitrobenzoic acids was usually effected by means of hot dilute nitric acid, which in all cases gave good yields (about 90%). (In the case of phenylbromocyanonitromethane, permanganate was also used.) The general method was to boil the nitration product with excess of nitric acid (*d* 1·10—1·15) for periods varying from 2—10 hours, according to the example under investigation. It was shown experimentally that benzoic acid is not nitrated under these conditions. On cooling the nitric acid solution, part of the

nitrobenzoic acids crystallised, and this portion was sometimes collected and treated separately. The remainder was extracted with pure ether and freed from nitric acid and colouring matter in the manner described by Holleman ("Die Direkt Einführung von Substitution in den Benzolkern," p. 121).

Estimation of the Proportion of m-*Nitrobenzoic Acid in the Mixed Nitrobenzoic Acids obtained by Oxidation of the Nitration Products.*—For this purpose, the mixed nitrobenzoic acids were reduced to aminobenzoic acids by means of titanous chloride and these were brominated with bromide–bromate solution under the conditions used by Goss, Ingold, and Wilson (*loc. cit.*) to estimate the proportion of meta-isomeride in nitrobenzylamine derivatives, except that in the present cases the bromination was effected at − 10°. Experiments with artificial mixtures of *o*-, *m*-, and *p*-nitrobenzoic acids showed that calculation of the meta-contents from the quantities of bromine absorbed on a strictly theoretical basis led to results about 4% too high on the average, and an empirical connexion between the meta-content and the bromination number *F* (*loc. cit.*) was therefore established in order to give the correction appropriate to various compositions:

Mixture.	*p*-.	*o*-, *p*-, *m*-.	*p*-, *m*-.	*o*-, *p*-, *m*-.	*p*-, *m*-.	*p*-, *m*-.	*m*-.
% meta- ...	0·0	18·0	40·5	48·3	71·2	90·6	100·0
F	2·089	2·263	2·422	2·516	2·763	2·931	3·000

Since all these points lie on or about a straight line, it is evident that the necessity for correction arises solely on account of the production of small amounts of *s*-tribromoaniline. The corrections to be applied to the theoretically calculated *m*-content are:

Apparent *m*-content (%)	30	40	50	60	70	85
Correction (%)	−6	−5	−4	−3	−2	−1

The results obtained by this method were confirmed by the separation of *m*-nitrobenzoic acid from the mixtures.

Separation of m-*Nitrobenzoic Acid from the Mixed Acids produced by Oxidation of the Nitration Products.*—The *m*-acid was separated from its isomerides by making use of the large differences in the solubility of the three isomerides in cold chloroform and the large solubility of the barium salt of the *o*-acid in cold water. The solubilities in question were taken as having the following values in g. per 100 g. of solvent:

	Ortho-.	Meta-.	Para-.
Acids in chloroform at 20°	1·09	4·07	0·101
Barium salts in water at 20° ...	Very sol.	0·377 (+$4H_2O$)	0·400 (+$5H_2O$)
„ „ „ 100° ...	„	5·2	12·5

A known weight of the mixture was triturated at 20° with rather more than sufficient chloroform to dissolve all the *m*-acid present,

the amount having previously been determined by reduction and bromination (above). In general, this quantity of chloroform was sufficient to dissolve all the ortho-compound present also; a small amount of the *p*-acid also dissolved, and the approximate quantity could be calculated from the solubility data given above. The undissolved portion usually consisted of practically pure *p*-nitrobenzoic acid. The chloroform extract was evaporated in a vacuum and the residual acids neutralised with standard barium hydroxide using phenolphthalein as an external indicator. The solution was then concentrated to a volume calculated to be sufficient to retain the whole of the salt of the *p*-acid in solution at 20°, and the *m*-salt, which crystallised at this temperature, was collected and washed with alcohol and ether. In some cases, the salt was recrystallised from a known quantity of water and washed as before. It was then dissolved in hydrochloric acid and the *m*-acid extracted with pure ether, any precipitated *m*-acid being collected separately in some cases. The extract was dried with sodium sulphate and evaporated, and the residual *m*-nitrobenzoic acid weighed. Allowance can be made for the small amounts of the barium salt of this acid retained in solution during the crystallisations. If any benzoic acid (arising from incomplete nitration of the original phenylnitromethane) is present, this separation is somewhat interfered with, the solubility of benzoic acid being about 14 g. in 100 g. of cold chloroform, and that of its barium salt about 5 g. in 100 c.c. of water, and in this case the m. p. of the separated *m*-nitro-acid may be 10—15° too low. It is, however, readily purified to an acid of the correct m. p. by crystallisation from a small volume of ethyl acetate–ligroin.

A mixture of nitrobenzoic acids containing ortho-, 0·105 g.; meta-, 0·485 g.; para-, 0·410 g. (total weight 1·000 g.) was triturated with 13·0 g. of chloroform, which should dissolve all the *o*- and *m*-acids present and about 0·013 g. of the *p*-acid. The undissolved residue weighed 0·380 g. and had m. p. 234—235° (para-). The dissolved *p*-acid is equivalent to 0·022 g. of barium salt, which is soluble in 5·5 c.c. of cold water. The acids remaining after evaporation of the chloroform (0·62 g.) were converted into barium salts, which were allowed to crystallise from 7·0 c.c. of water. The *m*-acid regenerated from the crystallised salt weighed 0·460 g. and had m. p. 135—137°. The weight corresponding with the meta-barium salt retained in solution is 0·013 g., and this may be applied as a correction:

Proportion of *m*-acid present = 48·5%
Proportion of *m*-acid isolated = 46·0%
Solubility correction = 1·3%
} Total 47·3%

The deficit is therefore 1·2%. In the case of mixtures obtained by the oxidation of nitration products, and analysed by the bromination method, the deficit was usually a little greater (mean, 2·5%).

(C) *Details relating to Individual Cases.*

1. *Phenylnitromethane.*—Holleman (see p. 2463), when nitrating this substance and isolating the *m*-nitro-derivative, did not establish the presence of any other isomeride, although the formation of the *o*-derivative was inferred from the taste of the nitrobenzoic acids obtained by oxidation of the residues. We find that the *p*-derivative is also formed, but we confirm Holleman's observation that the *m*-isomeride is the principal product.

Details peculiar to this case are as follows: (Expt. 2) Reagent: nitric acid (*d* 1·49). Temperature: 0°. Speed of addition: 1·0 g. per hour. The general method was followed except that the nitration product, which was precipitated in a crystalline form by pouring on ice, was collected by filtration, and the filtrate nearly neutralised with sodium hydroxide, then fully neutralised with precipitated calcium carbonate, and extracted with ether (yield 92% of theory) (Found: C, 45·3; H, 3·5. Calc.: C, 46·1; H, 3·3%). The remaining material was accounted for as acid products formed by oxidation.

Analysis: The nitrobenzoic acids (yield 91%), after reduction, absorbed bromine indicating an apparent meta-content of 52%; when corrected, this becomes 48%.

Separation: The separated *p*-nitrobenzoic acid had m. p. 233—234° (mixed m. p. 235°); yield 14%. The *m*-nitrobenzoic acid was collected in two portions. One (precipitated) had m. p. 140° (mixed m. p. 140°); yield 32%. The second (extracted from solution by ether) had m. p. 115—125° (mixed m. p. 135—140°), and when crystallised once from ligroin–ethyl acetate had m. p. 139° (mixed m. p. 140°); yield before crystallisation, 18%. Total yield of *m*-nitrobenzoic acid 50% (Found: C, 50·0; H, 3·3. Calc.: C, 50·3; H, 3·0%).

Since *m*-nitrophenylnitromethane crystallises well from glacial acetic acid an attempt was made to separate as much as possible from the nitration product. The mixture (0·635 g.) was crystallised from 1·0 c.c. of glacial acetic acid, and the mother-liquor decanted as completely as possible from the crystals, which were drained on porous porcelain. They weighed 0·261 g. and had m. p. 92° (the pure *m*-compound has m. p. 94°); yield 41%. By evaporation of the mother-liquors a further small quantity of impure *m*-compound, m. p. 70—75°, was obtained; yield 0·013 g. = 2%. Total amount separated, 42 ± 1%.

2. *Phenylbromocyanonitromethane.*—Flürscheim (see p. 2464) employed 8 parts of "fuming" nitric acid and conducted the nitration "in a freezing mixture." We have adhered to the same conditions (see below) in so far as they are specified by these statements. For the oxidation, Flürscheim used permanganate; we employed the same reagent, which gives a good yield, and also dilute nitric acid (Section B), with practically identical results. In order to ascertain whether the marked discrepancy between Flürscheim's results and our own (see pp. 2464—2465) in this important experiment was due to some accidental variation in the procedure, we repeated our experiments a number of times, using three different samples of initial material, and introducing several minor variations into the manipulation; the results, however, were sensibly the same.

(Expt. 24). Reagent: 8 parts of nitric acid (*d* 1·49). Temperature: — 15°. Rate of addition: 2·0 g. per hour. Material used: 13·0 g. of Sample B (analysis, Section A). After the addition, the mixture was kept at — 15° for 1·5 hours and at + 15° for 0·5 hour and then poured on ice. The mixture was nearly neutralised with potassium hydroxide and extracted with ether, and the extract washed five times with dilute sodium carbonate, dried with sodium sulphate, and evaporated in a vacuum over phosphorus pentoxide. Flürscheim describes his nitration product as an oil; ours partly crystallised. Flürscheim's yield is not recorded; our yield, in this experiment, was 75% of the theoretical, the remaining material having apparently undergone oxidation; 10% was recovered as acid products formed by oxidation.

Analysis: The nitrobenzoic acids, which were obtained in 86% yield by oxidation with dilute nitric acid (Section B) (Found: C, 49·6; H, 3·2. Calc.: C, 50·3; H, 3·0%), when analysed by reduction and bromination, gave an apparent *m*-content of 57%. The corrected proportion of *m*-isomeride is therefore 54%.

Separation: The separated *p*-nitrobenzoic acid had m. p. 215—220° (mixed m. p. 228—231°); yield 12%. The *m*-nitrobenzoic acid was collected in two portions. One (precipitated) had m. p. 133—136° (mixed m. p. 141°) and, after one crystallisation from ethyl acetate–ligroin, 140°; the other (extracted from solution) had m. p. 128—133° (mixed m. p. 139—140°) and, after one crystallisation, 141°; total yield 47%.

(Expt. 21). Material used: 5·8 g. of Sample A (analysis, Section A). Yield of nitration product, 70% of the theoretical (Found: C, 35·0; H, 1·9. Calc.: C, 33·6; H, 1·4%). Yield of nitrobenzoic acids obtained by oxidation with dilute nitric acid 79%. Analysis by the bromination method gave an apparent meta-content of 53%, which, on correction, corresponds with 50% of *m*-isomeride.

(Expt. 22). Material used : 7·1 g. of Sample A (analysis, Section A). In this experiment, the nitration product (yield 74%; yield of acid by-product, 14%) was washed with alcohol and so divided into a crystalline portion sparingly soluble and an oil readily soluble in alcohol. The crystalline portion (42% of the whole), on oxidation by dilute nitric acid to nitrobenzoic acids (yield 82%) (Found : C, 49·0; H, 3·1%), gave no *p*-acid and 58% of the *m*-acid (m. p. 130—135°; mixed m. p. 135—140°). The oily portion (58% of the whole) on oxidation (yield 82%) gave 28% of the *p*-acid, m. p. 200—210°; mixed m. p. 225—228° (Found : C, 49·1; H, 3·3%) and 26% of the *m*-acid (m. p. 133°; mixed m. p. 140—141°). The yield of *p*-acid calculated on the whole product is 16% and the yield of *m*-acid is 44%. Analysis by the bromination method gave a meta-content of 51% (corrected).

(Expt. 25). Flürscheim oxidised his material by means of permanganate, and in order to ascertain whether this method leads to selective destruction of the *m*-isomeride, we employed it also. Oxidation by 1% permanganate, added gradually to a suspension of the material in sodium hydrogen carbonate solution on the steam-bath, gave nitrobenzoic acids in 89% yield, and, from these, 50% of *m*-nitrobenzoic acid (m. p. 125—132°; mixed m. p. 139—140°).

The specimens of mixed nitrobenzoic acids obtained in these nitration products of phenylbromocyanonitromethane usually had the odour of benzoic acid and small amounts of this acid were separated by sublimation. Since the presence of benzoic acid, which Flürscheim also observed, indicates incomplete nitration of the original nitromethane derivative, it follows that the real proportion of *m*-substitution is probably slightly higher than is indicated by the yields of *m*-nitrobenzoic acid recorded above.

3. β-*Phenyl*-β-*nitropropane*.—Reagent : nitric acid (*d* 1·49). Temperature : — 15°. Rate of addition : 1·3 g. per hour. The mixture was kept for 3 hours at — 15° after completing the addition and then poured on ice.

(Expt. 38). Material used : 4·0 g. of Sample B (analysis, Section A). The yield of nitration product was 85%, and the whole of the remaining material (15%) was accounted for as acid products formed by oxidation. The yield of nitrobenzoic acids was quantitative. The separated *p*-nitrobenzoic acid had m. p. 225—227° (mixed m. p. 230—232°); yield, 38%. The *m*-acid was collected in two portions. One (precipitated) had m. p. 138—141° (mixed m. p. 141°); yield 14%. The other (extracted from solution) had m. p. 130—132° (mixed m. p. 135—138°); yield 7%. Total yield 21%.

(Expt. 33). Material used : 5·0 g. of Sample A (analysis, Section A). The yield of nitration product was 94% of the theoretical (Found : C, 50·7; H, 4·5. Calc. : C, 51·5; H, 4·8%). The yield of mixed nitrobenzoic acids was 95% (Found : C, 49·9; H, 3·6%). The separated *p*-nitrobenzoic acid had m. p. 215—222° (mixed m. p. 234—236°) and, when crystallised, had m. p. 232—234°; yield 35%. The *m*-acid commenced to soften at 125° and melted at 140°; yield 35%.

(Expt. 37). Material used : 3·8 g. of Sample A. The percentage yields at each stage were identical with those of Expt. 38, except that the total yield of *m*-acid was 26%.

(Expt. 39). The nitration product (Found : C, 52·4; H, 4·5%) on oxidation gave nitrobenzoic acids (Found : C, 49·3; H, 3·0%) in 95% yield. The proportion of *m*-acid found by the bromination method was 29% (corrected).

4. *α-Phenyl-α-bromo-α-nitroethane.*—Considerable difficulty was experienced in obtaining a completely nitrated product, but ultimately the following process was adopted : (Expt. 44). 3 G. of the nitroethane were run during 2·25 hours into 4·5 g. of nitric acid (*d* 1·49) at 15°, and the product was kept for a further 2·25 hours at this temperature before pouring on ice. A considerable amount of oxidation took place, and the nitration product, which was isolated in only 40% yield (Found : C, 37·4; H, 3·0), gave nitrobenzoic acids in a yield of 80%. The separated *p*-acid had m. p. 220—225° (mixed m. p. 232°); yield, 25%. The *m*-acid was obtained in two portions. One (precipitated) had m. p. 134—135° (mixed m. p. 141°) and, after crystallisation from ligroin–ethyl acetate, 141°; yield 24%. The second (extracted from solution) had m. p. 125—130° (mixed m. p. 140°) and after crystallisation melted at 137° (yield 14%) (Found : C, 49·4; H, 3·1%). The total yield of *m*-acid was therefore 38%. The proportion of *m*-isomeride was not determined by bromination in this case, and in the table in Section D the above value is rounded to 40% since the average loss of *m*-acid during these separations is calculated to be 2·5%. These figures are regarded as approximate only.

5. *Phenyldibromonitromethane.*—Reagent : nitric acid (*d* 1·49). Temperature : — 15°. Rate of addition : 2 g. per hour. After the addition was complete, the mixture was kept at — 15° for a further 3 hours and then poured on ice and worked up as usual.

(Expt. 52). Material : 5·0 g. of sample A (analysis, Section A). Yield of nitration product, 88% of the theoretical (Found : C, 25·1; H, 1·7. Calc. : C, 24·7; H, 1·2%).

Analysis : A portion of the nitration product, on oxidation, gave an 87% yield of mixed nitrobenzoic acids (Found : C, 49·7;

H, 3·0%). Reduction and bromination gave an apparent *m*-content equal to 85%, which on correction becomes 84%.

Separation: A second portion of the same nitration product was oxidised, and the yield of mixed nitrobenzoic acids was in this case 100% (Found: C, 50·9; H, 3·5%). The separated *p*-acid had m. p. 221° (yield 6%). The *m*-acid had m. p. 120—125° (mixed m. p. 137—139°) (yield 80%).

(Expt. 53). Material: 5·3 g. of sample B (analysis, Section A). Yield of nitration product, 87% (Found: C, 25·5; H, 1·3%).

Analysis: Oxidation gave nitrobenzoic acids in 93% yield. Reduction and bromination of these gave 85% of *m*-isomeride (corrected).

Separation: Yield of separated *p*-acid, 6%. The separated *m*-acid was collected in two fractions: precipitated portion (m. p. 138—139°; mixed m. p. 141°), 60%; extracted portion (m. p. 125°; mixed m. p. 134—139°), 19%. The extracted portion after one crystallisation melted at 136—138° (mixed m. p. 141°). Total yield of *m*-acid 79%.

(D) *Summary of Results.*

The following tabular summary is appended for convenience in reference.

Nitration of Phenylnitromethanes by Nitric Acid (d 1·49).

RR′ in directing group, $CRR'\cdot NO_2$.	Temp.	Conversion to nitrobenzoic acids (%).	Separation of isomerides (%). *Para*-.	Mean.	*Meta*-.	Mean.	% *Meta*- (by estimation).	Mean % *meta*-.
Me,Me	−15°	98	38 35 38	37	21 35 26	27	29	29
Me,Br	+15	80	25	25	38	38	—	40
H,H	± 0	91	14	14	50	50	48	48
CN,Br	−15	84	12 — 16 —	14	47 — 44 50	47	54 50 51 —	52
Br,Br	−15	93	— 6 6	6	— 80 79	79	84 — 85	84

The rough parallelism between the successive decreases in *para*- and increases in *meta*-, on passing through the series, is noteworthy.

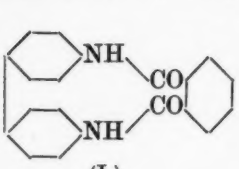
We desire to thank the Royal Society for defraying part of the expense incurred in this research.

THE UNIVERSITY, LEEDS. [*Received, July 6th*, 1926.]

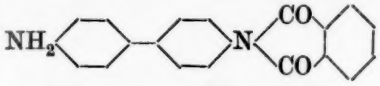
CCCXXVI.—*The Space Formula of Diphenyl.*

By Raymond James Wood Le Fèvre and Eustace Ebenezer Turner.

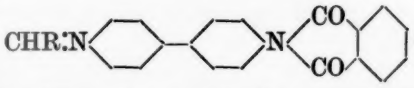
In a recent communication (Le Fèvre and Turner, this vol., p. 2042), it was recorded that, when monophthalylbenzidine is nitrated, the main product is the 2- and not, as stated by Koller (*Ber.*, 1904, **37**, 2882), the 3-nitro-derivative. It occurred to us at the time that, although the formula (I) hitherto assigned to monophthalylbenzidine does not enable one to predict, with any degree of certainty, the orientation of the mononitro-compound, formula (II) would do so adequately, in view of the well-known meta-directing influence of the amino-sulphate group. In accordance with this formula (II) monophthalylbenzidine dissolves in boiling benzaldehyde and salicylaldehyde, the solutions on cooling depositing *benzylidene-* and *salicylidene-monophthalylbenzidine*, respectively (III). Moreover,



(I.)



(II.)

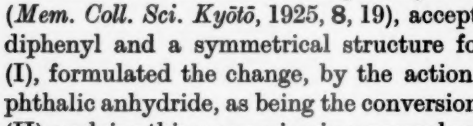


(III.)

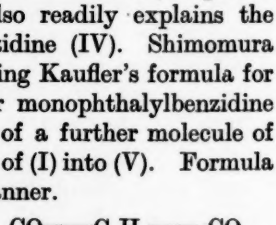
although monophthalylbenzidine is apparently reprecipitated unchanged when its solution in concentrated sulphuric acid is diluted, the product is actually the *sulphate*,

$$(C_6H_4{\cdot}C_2O_2{\cdot}N{\cdot}C_6H_4{\cdot}C_6H_4{\cdot}NH_2)_2,H_2SO_4.$$

Finally, monophthalylbenzidine may be diazotised in concentrated sulphuric acid solution to give a sparingly-soluble solid *diazonium sulphate*, which is very stable and couples with alkaline β-naphthol to form a red *azo-dye*. Formula (II) also readily explains the conversion of mono- into di-phthalylbenzidine (IV). Shimomura (*Mem. Coll. Sci. Kyōtō*, 1925, **8**, 19), accepting Kaufler's formula for diphenyl and a symmetrical structure for monophthalylbenzidine (I), formulated the change, by the action of a further molecule of phthalic anhydride, as being the conversion of (I) into (V). Formula (II) explains this conversion in a normal manner.



(IV.)

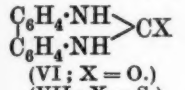


(V.)

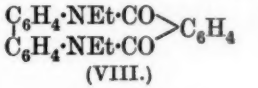
Kaufler (*Annalen*, 1907, **351**, 151; *Ber.*, 1907, **40**, 3250) advanced his formula for diphenyl compounds in order to account for the

existence of a number of derivatives of benzidine "in which the amino-groups were linked either through one or two neighbouring carbon atoms." *

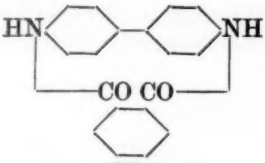
The actual examples he cited were carbonylbenzidine (Michler and Zimmermann, *Ber.*, 1881, **14**, 2178), thiocarbonylbenzidine (Borodine, *Jahresb.*, 1860, 356; Strakosch, *Ber.*, 1872, **5**, 240), diethylphthalylbenzidine (Schiff and Vanni, *Annalen*, 1890, **258**, 363), monophthalylbenzidine (Koller, *loc. cit.*) and oxalylbenzidine,† to which substances the original discoverers had already assigned formulæ (VI), (VII), (VIII), (IX), and (X), respectively.



(VI; X = O.)
(VII; X = S.)



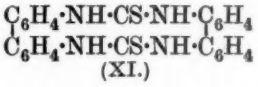
(VIII.)



(IX.)

$C_{12}(C_2O_2)H_{10}N_2$

(X.)



(XI.)

Kaufler made the assumption that the two benzene nuclei in diphenyl are inclined towards each other ("gegen einander geneigt"), and not that they are parallel, as is usually stated, although in his formulæ the 1 : 1′- and 4 : 4′-positions are represented as being equidistant. His formulæ for the above compounds merely had the benzene ring written instead of the grouping C_6H_4. Strakosch recognised the possibility that thiocarbonylbenzidine might be (XI), but owing to the insolubility of this compound he was unable to determine its molecular weight. The new experimental evidence published by Kaufler (as far as diphenyl derivatives are concerned), consisted of determinations of the molecular weights of monophthalylbenzidine, monophthalyldianisidine and thiocarbonyldianisidine, the last two compounds only being prepared by him. He therefore doubted, not the mode of linking of the amino-groups, but what he termed the "unimolecular" nature of the compounds. For, finding that the molecules of the above three substances contained only one benzidine residue, he concluded that "for the other derivatives named, an analogous constitution was made very probable."

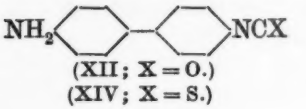
The discovery that monophthalylbenzidine, the most fully investigated Kaufler compound, has a constitution other than that

* Kaufler also considered that naphthalene and other polynuclear molecules had folded configurations. It is hoped to deal with these in a subsequent communication.

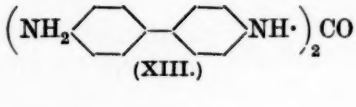
† For this substance Kaufler gives two references: Borodine, *Jahresb.*, *loc. cit.*, and Strakosch, *loc. cit.* The latter paper contains no mention of oxalylbenzidine; the *Jahresb.* contains only a brief abstract. The correct reference is *Z. Chem. Pharm.*, 1860, 641.

hitherto assumed, made it imperative to examine a number of other compounds of a supposedly similar structure. Carbonyl- and thiocarbonyl-benzidine were therefore prepared by the methods described in the literature.

The former was found to form a *sulphate*, and to condense with aromatic aldehydes, and therefore to contain a free amino-group. In view of the fact that the interaction of carbonyl chloride and amines usually leads to the production either of carbamyl chlorides or of carbamides, it appears probable that carbonylbenzidine is (XIII) rather than (XII), since carbimides are usually only produced by the action of carbonyl chloride on amine hydrochlorides at comparatively high temperatures. This view, which cannot be



(XII; X = O.)
(XIV; X = S.)



(XIII.)

completely substantiated, owing to the insolubility of carbonylbenzidine in cryoscopic or ebullioscopic solvents, is supported by the observation that carbonylbenzidine is apparently unaffected by boiling aniline. In any case, formula (VI) is excluded.

Thiocarbonylbenzidine has been found definitely to have formula (XIV).* As an amine, it condenses with aldehydes, and, as a thiocarbimide, it is converted by aniline into *4′-aminodiphenylylphenylthiocarbamide*, $NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot NH \cdot CS \cdot NHPh$, and by phenol into *phenyl 4′-aminodiphenylylthiocarbamate*,

$$NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot NH \cdot CS \cdot OPh.$$

Further, although thiocarbonylbenzidine is stated in the literature (*loc. cit.*) to be precipitated unchanged when its solution in concentrated sulphuric acid is diluted, the precipitate actually consists of the *sulphate*, $(SCN \cdot C_6H_4 \cdot C_6H_4 \cdot NH_2)_2, H_2SO_4$.

It seems probable that the condensation products discussed by Kaufler are the substances that are isolated mainly because of their extreme insolubility. An interesting example of the formation of a mono-derivative under conditions where a di-derivative was expected is given, without reference to the present problem, by von Auwers (*Annalen*, 1896, **292**, 177): benzidine was heated in benzene solution with two molecules of tetramethylsuccinic anhydride; compound (XV) then separated almost quantitatively. In this

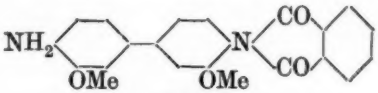
* Reuland (*Ber.*, 1889, **22**, 3014) found that diphenyline (2 : 4′-diaminodiphenyl) was converted by alcoholic carbon disulphide into a compound which he called thiocarbonyldiphenyline, and wrote as (VII) with complete benzene rings. There is little doubt that the substance is actually an aminodiphenylylthiocarbimide, analogous to (XIV).

particular case the product formed a soluble hydrochloride and was thus recognised as a base.

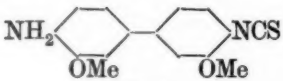
(XV.) $NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot N\langle \begin{matrix} CO \cdot CMe_2 \\ CO \cdot CMe_2 \end{matrix}$ $\qquad$ $\begin{matrix} C_6H_4 \cdot NH_3 \\ C_6H_4 \cdot NH_3 \end{matrix} \rangle SO_4$ (XVI.)

Whereas benzidine dihydrochloride is soluble in water, the monohydrochloride is sparingly soluble (Schmidt and Schultz, *Annalen*, 1881, **207**, 330), and therefore we suggest that benzidine sulphate has the formula $NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot NH_3 \cdot HSO_4$ rather than (XVI).

There seems no reason to doubt that Kaufler's monophthalyl- and thiocarbonyl-dianisidine are respectively (XVII) and (XVIII); this



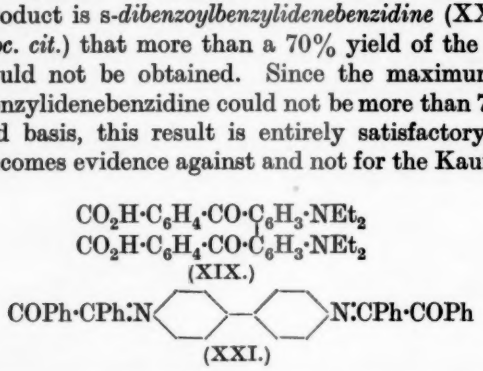
(XVII.)



(XVIII.)

author's molecular-weight determinations support these structures and the structure (II) assigned to monophthalylbenzidine as well as they do the formulæ he suggested. Of the other Kaufler compounds mentioned above, there remain to be considered oxalylbenzidine and diethylphthalylbenzidine. The former has been found (qualitatively) to condense with benzaldehyde and thus to contain a free amino-group or groups, whilst the latter, although apparently a condensation product, with phthalic anhydride, of a compound containing no primary amino-group—therefore furnishing the most convincing evidence adduced by Kaufler in favour of his formula—was not a chemical individual. Schiff and Vanni (*loc. cit.*), who first described it, heated phthalic anhydride with "diethylbenzidine" and assigned formula (VIII) to the product. At the same time, tetraethylbenzidine was stated to give the compound (XIX). P. Hofmann (*Annalen*, 1860, **115**, 365) first ethylated benzidine, obtaining a "diethylbenzidine" melting at 65°. This was presumably the material used by Schiff and Vanni, since they say nothing about the preparation of their specimen. It was evidently regarded by Beilstein (compare "Handbuch," 3rd ed., Vol. IV, 967, 963) as the symmetrical diethyl derivative. Bamberger and Tichwinsky (*Ber.*, 1902, **35**, 4179) found that symmetrical diethylbenzidine melted at 115·5° and isolated it from the product obtained by Hofmann's process. Later, Tichwinsky (*J. Russ. Phys. Chem. Soc.*, 1903, **35**, 675) showed that this product was a mixture of 15% of tetra- and 85% of *s*-di-ethylbenzidine. It is therefore evident that no conclusions whatever can be drawn from Schiff and Vanni's results.

Cain (J., 1914, **105**, 1437) described a condensation product of benzidine and benzil, assumed to have formula (XX), which he was unable to free from methyl or ethyl alcohol of crystallisation. Ferriss and Turner (J., 1920, **117**, 1140) showed that the condensation product could readily be obtained free from solvent of crystallisation, but failed to realise what is now evident, that the condensation product is s-*dibenzoylbenzylidenebenzidine* (XXI). It was observed (*loc. cit.*) that more than a 70% yield of the condensation product could not be obtained. Since the maximum yield of dibenzoylbenzylidenebenzidine could not be more than 74%, calculated on the old basis, this result is entirely satisfactory and the experiment becomes evidence against and not for the Kaufler formula.



Adams, Bullock, and Wilson (*J. Amer. Chem. Soc.*, 1923, **45**, 521) condensed *iso*- and tere-phthalaldehydes with benzidine and obtained amorphous compounds which were regarded as of the " unimolecular " type, without any supporting experimental evidence being put forward. We have not examined these substances, as they do not affect the position.

Similarly, the diazoimides obtained by Vaubel and Scheuer (*Z. Farb. Tech. Ind.*, 1906, **5**, 61) were, from the description given, ill-defined compounds of unknown molecular complexity, and it is difficult to see on what lines they could be examined from the point of view of the present paper.

Morgan and Micklethwait (J., 1908, **93**, 614) found that whilst naphthalene-β-sulphonylbenzidine was readily convertible into a substance which they formulated as (XXII) or (XXIII), *as*-naphthalene-β-sulphonylethylbenzidine, $NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot NEt \cdot SO_2 \cdot C_{10}H_7$, could not be converted into a similar substance, a result which

(XXII.) $\begin{matrix} C_6H_4 \cdot NH \cdot NO, H_2O \\ C_6H_4 \cdot NH \cdot SO_2 \cdot C_{10}H_7 \end{matrix}$ $\qquad$ $\begin{matrix} C_6H_4 \cdot N_2 \\ C_6H_4 \cdot N \cdot SO_2 \cdot C_{10}H_7, 2H_2O \end{matrix}$ (XXIII.)

supports formula (XXIII) rather than (XXII). The presence of water of crystallisation, however, makes a decision uncertain, as the authors pointed out (compare also Kenner and Mathews, J., 1914, **105**, 2473), and the meaning of this work as regards the Kaufler

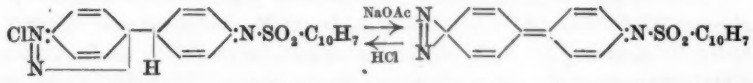
formula is not clear. The compound,* like that from benzenesulphonylbenzidine (Morgan and Hird, J., 1905, **91**, 1505), is a crystalline substance differing from most of Kaufler's compounds in appearance.

The most important phenomena in connexion with which the Kaufler formula has been discussed are, first, the isomerism of the dinitrobenzidines (Cain, Coulthard, and Micklethwait, J., 1912, **101**, 2998, etc.) and of the 6 : 6′-dinitrodiphenic acids (Kenner and Stubbings, J., 1921, **119**, 593), and, secondly, the optical activity of the substituted diphenic acids (Christie and Kenner, J., 1922, **121**, 614, etc.). The former phenomena have been shown not to exist (Le Fèvre and Turner, this vol., p. 1759; Christie, Holderness, and Kenner, *ibid.*, p. 671), whilst the explanation of the second, well-established phenomenon has still to be discovered.

Kaufler (*loc. cit.*) considered that his formula explained not only the reactions of benzidine already discussed, but also, on the assumption of steric hindrance between groups in the 4- and 4′-positions, (1) the difficulty of diazotising the second amino-group in benzidine, (2) the slowness of coupling of the second diazo-group in diphenylbisdiazonium salts, and (3) the benzidine change. As has been pointed out by Vignon (*Compt. rend.*, 1906, **142**, 159) and by Cain ("Chemistry and Technology of Diazo Compounds," 1920, p. 27), difficulty (1) does not exist. The second point would appear to be sufficiently explained by the insolubility of the intermediate monoazo-dye produced during the coupling of bisdiazotised benzidine (compare Georgevics and Grandmougin, "Text-book of Dye Chemistry," trans. by Mason, 1920, p. 129, for many technical applications).

As regards the benzidine change, we are unable to see any advantage in Kaufler's formulation, which, incidentally, does not explain the formation of diphenyline. We are also unable to understand why Raiford and Clark (*J. Amer. Chem. Soc.*, 1926, **48**, 483) should, on the basis of the Kaufler formula, have expected 4-amino-4′-hydroxydiphenyl to behave, as regards migrations of its acyl derivatives, like *o*-aminophenol.

* Professor Morgan informs me that he now regards the scheme



as explaining more satisfactorily the formation and properties of the naphthalenesulphonyl derivative. This explains why a similar compound is not obtained from the ethyl derivative, and would appear to remove the last remaining evidence in favour of Kaufler's formula.—E. E. T.

Kuhn and Zumstein (*Ber.*, 1926, **59**, 488) determined the dissociation constant of benzidine and compared it with the corresponding values for the three phenylenediamines; their conclusion is that the amino-groups in benzidine are farther apart than Kaufler's formula suggests.

The views expressed by one of us in 1915 (J., **107**, 1495) would thus appear to be fully justified, since the inconsistencies then referred to have now been explained. We do not regard the present work as proving anything beyond the fact that there is no satisfactory evidence for the existence of compounds of the type to be expected if Kaufler's formula for diphenyl were the correct one. At the same time, since no authentic cases of "*cis-trans*" isomerism are known to occur among the diphenic acids capable of resolution, it would probably be justifiable to regard our results as indicating that the diphenyl molecule has not a folded structure. It seems very unlikely that the cause of stereoisomerism in the diphenyl series is a mere matter of the angle between the two benzene nuclei.

Experimental.

Monophthalylbenzidine (II) prepared by Koller's method (*loc. cit.*) was repeatedly extracted with alcohol and crystallised from phenol (Found: N, 9·0. Calc.: N, 8·9%). The latter solvent is readily removed from the solid, whereas nitrobenzene, recommended by Koller, is tenaciously retained.

Monophthalylbenzidine dissolved in concentrated sulphuric acid with a slight evolution of heat. The brown solution was poured into a large bulk of water, the bluish-grey *sulphate* precipitated was filtered off, thoroughly extracted with boiling water, and dried at 100° [Found: N, 7·8. $(C_{20}H_{14}O_2N_2)_2,H_2SO_4$ requires N, 7·7%].

Benzylidene- and Salicylidene-monophthalylbenzidine (III).—Monophthalylbenzidine (1 g.) was heated with 25 c.c. of the appropriate aldehyde, the condensed water being removed in the usual manner from time to time. When the whole of the monophthalylbenzidine had dissolved, the solution was filtered; on cooling, it set to a solid magma. The filtered crystals were washed first with the parent aldehyde, then with alcohol, and dried at 100°.

Benzylidenemonophthalylbenzidine forms yellow needles, m. p. above 300° (Found: N, 7·3. $C_{27}H_{18}O_2N_2$ requires N, 7·0%). *Salicylidenemonophthalylbenzidine*, microscopic platelets, melts above 300° (Found: N, 6·6. $C_{27}H_{18}O_3N_2$ requires N, 6·7%). It is hydrolysed by boiling alkali or acid.

Diazotisation of Monophthalylbenzidine.—A solution of 5 g. of monophthalylbenzidine in 50 c.c. of concentrated sulphuric acid was treated gradually at −10° to −5° with the calculated quantity of

solid sodium nitrite. Dilution, by addition of ice, gave a yellow paste of the *diazonium sulphate*, which was insoluble in water. When it was added to sodium β-naphthoxide solution, a deep red *azo-dye* was formed, and coated the sulphate. The diazonium sulphate is recovered unchanged when shaken with a solution of bromine in hydrobromic acid. As Armstrong has pointed out (P., 1899, **15**, 176), diazosulphanilic acid also is indifferent to the action of the same reagent.

Carbonylbenzidine (XIII) was prepared as described by Michler and Zimmermann (*loc. cit.*) and purified by sublimation in a current of carbon dioxide (Found: N, 13·6. Calc.: N, 13·3%). Addition of its solution in concentrated sulphuric acid to an excess of water led to the precipitation of the whitish-yellow *sulphate* (Found: N, 10·9. $C_{25}H_{22}ON_4,H_2SO_4$ requires N, 11·4%).

The *salicylidene* and *benzylidene* derivatives were sparingly soluble in the respective aldehydes, from which they separated as yellow powders. Salicylidene derivative: Found, N, 9·0. $C_{39}H_{30}O_3N_4$ requires N, 9·3%. Benzylidene derivative: Found, N, 9·6. $C_{39}H_{30}ON_4$ requires N, 9·8%.

Thiocarbonylbenzidine (XIV), prepared as described by Strakosch (*loc. cit.*), was purified by repeated extraction with boiling methylated spirit (Found: N, 13·0. Calc.: N, 12·4%). When its solution in sulphuric acid was added to an excess of water, the *sulphate* was precipitated as a grey powder, which, after being well washed, was dried at 100° [Found: N, 9·4. $(C_{13}H_{10}N_2S)_2,H_2SO_4$ requires N, 10·1%]. When boiled with the appropriate aldehyde, thiocarbonylbenzidine was converted into the *benzylidene* derivative (Found: N, 8·3. $C_{20}H_{14}N_2S$ requires N, 8·9%), and the *salicylidene* derivative (Found: N, 8·4. $C_{20}H_{14}ON_2S$ requires N, 8·5%).

Acetylthiocarbonylbenzidine.—The suspension obtained by heating thiocarbonylbenzidine under reflux for one day with an excess of acetic anhydride and a trace of sulphuric acid was poured into water; after the acetic anhydride had decomposed, the cream-coloured solid was boiled with alcohol and dried at 100° (Found: N, 11·1. $C_{15}H_{12}ON_2S$ requires N, 10·5%).

Diazotisation of Thiocarbonylbenzidine.—A solution of thiocarbonylbenzidine in concentrated sulphuric acid (10 parts) was treated at 0° with water until the sulphate began to be precipitated. It was then diazotised with solid sodium nitrite. On dilution, a sparingly soluble, bright orange *diazo*-compound was precipitated, which coupled with alkaline β-naphthol solution to give a red *azo-dye*.

Phenyl 4′-Aminodiphenylylthiocarbamate. — Thiocarbonylbenzidine (2 g.) was boiled under reflux with 40 g. of phenol for 8 hours. It gradually became white and assumed a crystalline appearance.

The suspension was diluted with alcohol, filtered, and the product washed repeatedly with water and hot methylated spirit. The *thiocarbamate* was thus obtained as a white powder, m. p. above 300° (Found : N, 9·0. $C_{19}H_{16}ON_2S$ requires N, 8·7%).

4′-Aminodiphenylylphenylthiocarbamide. — Thiocarbonylbenzidine was boiled under reflux with an excess of aniline for 1 hour. The solution was poured into water, and dilute hydrochloric acid added until the grey precipitate was quite hard. It crystallised from much glacial acetic acid as a grey, microcrystalline powder (Found : N, 12·9. $C_{19}H_{17}N_3S$ requires N, 13·2%).

Action of Benzaldehyde on Oxalylbenzidine.—Oxalylbenzidine, prepared by Borodine's method (*loc. cit.*), was heated under reflux for a short time with benzaldehyde. Water was formed.

One of us is indebted to the Research Fund Committee of the Chemical Society for a grant in aid of this investigation.

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University of London. [*Received, June 29th*, 1926.]

CCCXXVII.—*The Alkaline Hydrolysis of Esters in Aqueous Alcoholic Solution. Part I. The Interaction of Phenoxides and Aliphatic Esters in Alcoholic Solution.*

By Eric Stephen Gyngell.

It was found by Creasy (unpublished work) that when sodium β-naphthoxide and ethyl acetate were allowed to react in alcoholic solution, β-naphthol and sodium acetate were the principal products, ethyl ether and naphthyl acetate being obtained in small quantity. These results were interpreted as showing that the reaction had taken place according to the equations,

$$(1)\ C_{10}H_7\cdot ONa + Et\cdot OH \rightleftharpoons C_{10}H_7\cdot OH + NaOEt,$$
$$(2)\ CH_3\cdot CO_2Et + NaOEt \longrightarrow CH_3\cdot CO_2Na + Et_2O.$$

Robertson and Acree (*Amer. Chem. J.*, 1913, **49**, 474) drew the similar conclusion that the reaction between sodium ethoxide and phenol did not proceed to completion in the formation of phenoxide. Cox (J., 1918, **113**, 666; 1920, **117**, 493), Haywood (J., 1922, **121**, 1904), and Segaller (J., 1913, **103**, 1104) have investigated reactions involving similar equilibria, without drawing any definite conclusion as to the importance or position of the equilibrium point. The velocity coefficients obtained by these workers show a slight

decline in value as the reaction proceeds. This has been taken as evidence in favour of the view that slight alcoholysis has taken place. This decrease in value is not larger than that obtained by Hecht, Conrad, and Brückner (*Z. physikal. Chem.*, 1891, **7**, 274) in their researches on the reaction between sodium ethoxide and alkyl iodides in alcoholic solution. There is no possibility of alcoholysis in this reaction and the slight decrease in the value of the velocity coefficients may be due to hydrolysis of the ethoxide by water present in the solution. (See also, Walker and Kay, J., 1897, **78**, 489; Kreman, *Monatsh.*, 1905, **26**, 279; and Senter, J., 1915, **107**, 1070.)

It was noticed by Cajola (*Gazzetta*, 1900, **30**, i, 233) that the saponification of methyl acetate by various bases in absolute methyl alcohol was not strictly bimolecular, and that the reaction appeared to cease before all the ester had been used. This has been interpreted by Cashmore, McCombie, and Scarborough (J., 1923, **123**, 197) as due to the degree of ionisation of the bases employed and to the stability of certain complexes. It is postulated that the reaction $CH_3{\cdot}OH + MOH \rightleftharpoons CH_3{\cdot}OM + H_2O$ cannot adjust itself with sufficient speed for the main reaction to go to completion or for bimolecular laws to be obeyed.

In the present work, it was considered desirable to conduct a series of preliminary experiments with a view to elucidate the conditions obtaining in alcoholic solutions of phenoxides. These experiments were at first conducted on the usual lines for velocity of reaction measurements. At 70° in ordinary absolute alcohol solution and with $N/2$-solutions, the time for half-reaction was considerably more than 10 hours. It was also evident that the reaction did not obey the simple bimolecular law which should have been followed had the course of the reaction been mainly :

1. $C_6H_5{\cdot}ONa + CH_3{\cdot}CO_2Et \longrightarrow C_6H_5{\cdot}OEt + CH_3{\cdot}CO_2Na.$

As a result of alcoholysis, there was also the possibility of the following reaction :

2. $CH_3{\cdot}CO_2Et + EtONa \longrightarrow Et_2O + CH_3{\cdot}CO_2Na.$

Conceivably both these reactions could take place at the same time, the extent depending somewhat upon the degree of alcoholysis of the phenoxide.

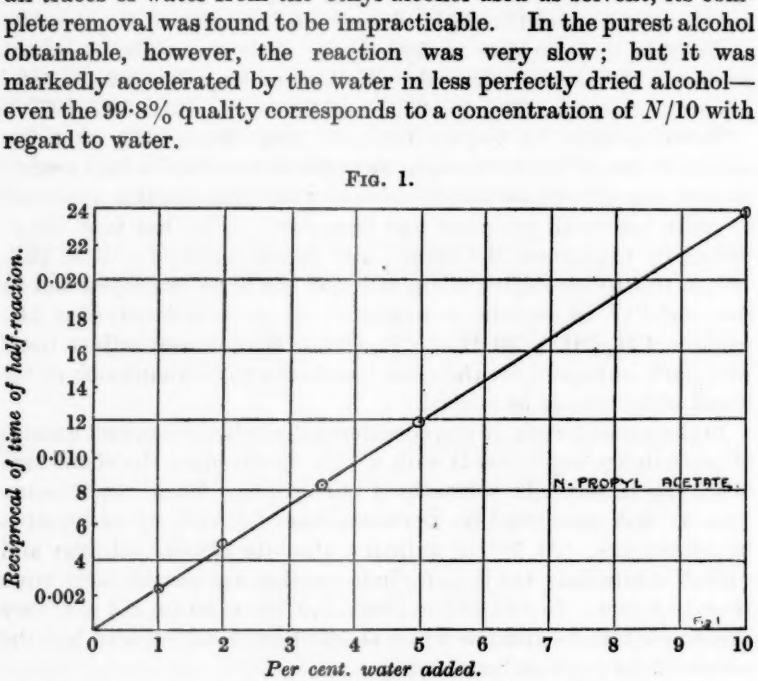
In general, the reaction yielded neither phenetole nor ether, and therefore did not proceed according to either of the above equations. Sodium acetate and phenol were, however, produced in quantity. In a few cases, notably with methyl and ethyl oxalates, anisole and phenetole, respectively, were produced in quantity, and the reaction proceeded much more rapidly than with esters of the acetic acid

series. No phenyl ether was produced from malonic or succinic esters with the possible exception of dimethylmalonic esters.

The Rôle of Water in Alcohol.

Although elaborate precautions were taken to remove and exclude all traces of water from the ethyl alcohol used as solvent, its complete removal was found to be impracticable. In the purest alcohol obtainable, however, the reaction was very slow; but it was markedly accelerated by the water in less perfectly dried alcohol—even the 99·8% quality corresponds to a concentration of $N/10$ with regard to water.

FIG. 1.



By using very pure alcohol, it was hoped to show that the velocity of the reaction was zero in the absence of water. It was not possible, however, to demonstrate this directly by experiment, but by plotting the reciprocal of the time of half-reaction against the amounts of water added (Fig. 1), it was shown that the curve passed through the origin, thus indicating that the reaction would not proceed if the complete removal of water could be effected.

The form of the reaction curves suggested the intervention of an equilibrium. It was thought that an intermediate additive compound between the ester and the sodium phenoxide, similar to that produced in the formation of acetoacetic ester, might be formed, but no evidence could be obtained for this supposition. The postulation of a hydrolytic equilibrium, however, provided a satisfactory hypothesis, since it explained the form of the curves, and

the effects of water in accelerating and of phenol in retarding the reaction. Thus, if the equilibrium and subsequent reaction are :

$$\underset{(c-x-y)}{C_6H_5\cdot OK} + \underset{(b-x-y)}{H_2O} \rightleftharpoons \underset{(d+x+y)}{C_6H_5\cdot OH} + \underset{y}{KOH}.$$

$$\underset{(a-x)}{CH_3\cdot CO_2Et} + \underset{y}{KOH} \longrightarrow \underset{x}{CH_3\cdot CO_2K} + \underset{x}{EtOH}.$$

where a, b, c, and d are the initial concentrations of ester, water, phenoxide, and phenol, respectively, and x is the amount of potassium acetate formed and y is the amount of free potassium hydroxide present at time t; then the concentrations of the reacting molecules are as shown, and, for equilibrium,

$$K(c-x-y)(b-x-y) = (d+x+y)y \quad . \quad . \quad . \quad (1)$$

where K is the equilibrium constant. For the saponification of the ester,

$$dx/dt = k(a-x)y \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

k being the velocity coefficient. It must now be assumed that y is always very small compared with x, *i.e.*, that the alkali formed by hydrolysis is always at a negligibly small concentration. Combining (1) and (2) and eliminating y, we obtain

$$dx/dt = Kk(a-x)(b-x)(c-x)/(d+x) \quad . \quad . \quad (3)$$

which on integration yields

$$Kkt = \frac{d+a}{(b-a)(c-a)}\log_e\frac{a}{a-x} + \frac{d+b}{(a-b)(c-b)}\log_e\frac{b}{b-x} + \frac{d+c}{(a-c)(b-c)}\log_e\frac{c}{c-x} \quad (4)$$

Similarly, when the ester and phenoxide are present in equivalent amounts we obtain

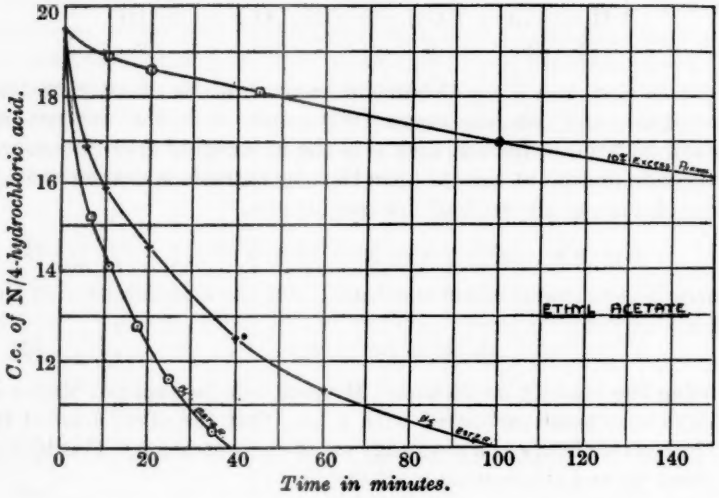
$$Kkt = \frac{d+b}{(b-a)^2}\log_e\frac{b(a-x)}{a(b-x)} + \frac{a+d}{b-a}\cdot\frac{x}{a(a-x)} \quad . \quad . \quad (5)$$

These formulæ were applied to the experiments performed with potassium phenoxide and ethyl acetate in alcoholic solution with satisfactory results. Formula (5) was, however, later modified to correct for the difference between the practical and the theoretical zero of the reaction. The formula used was

$$Kk(t_2-t_1) = \frac{b}{(b-a)^2}\log_e\frac{(a-x_2)(b-x_1)}{(a-x_1)(b-x_2)} + \frac{1}{b-a}\left\{\frac{x_2}{a-x_2} - \frac{x_1}{a-x_1}\right\} \quad . \quad . \quad (6)$$

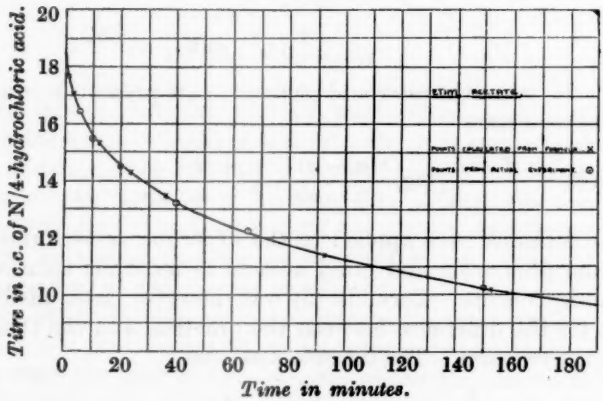
where the initial amount of phenol is zero. Actually it was found that the values of the coefficients obtained from this formula differed but little from those obtained from formula (5).

FIG. 2.



It will be seen that the velocity is proportional to the product (ester)(phenoxide)(water)/(phenol), and the effect of varying the concentration of the reactants is shown in Fig. 2. Fig. 3 shows

FIG. 3.



the experimental points and also the theoretical curve for a solution containing $N/2$-phenoxide and ester with 5% by volume of added water.

In a few cases it has been found possible to calculate the amount of water present in a solution containing no added water, and to use this calculated quantity for the determination of the velocity coefficients with satisfactory results.

Experimental.

Preparation of Potassium Phenoxide Solutions.—The phenoxide solutions employed were prepared by the method described by Robertson and Acree, except that it was impracticable to remove xylene from the metallic potassium by washing with absolute alcohol. Good potassium balls were therefore obtained practically free from incrustations. These balls were scraped clean under xylene, rapidly dried between filter-papers, and added to specially dried absolute alcohol under a reflux condenser. The condenser was fitted with a calcium chloride drying-tube, and the flask containing the alcohol was cooled by cold water. In this way it was found that phenoxide solutions could be prepared free from suspended matter, and showing scarcely any coloration even after standing for several weeks.

The ethoxide solution was titrated with standard acid, and the calculated amount of phenol was dissolved in alcohol and added to it; the whole was then diluted with alcohol to the required strength (usually N).

Purification of Alcohol.—The method employed consisted in refluxing alcohol with good, freshly-burnt quicklime for several days. It was thus possible to obtain alcohol of conductivity less than $0{\cdot}1 \times 10^{-6}$ at 25°. Loss of alcohol due to the wetting of the lime was reduced by using the lime successively for increasingly damp alcohol.

Preparation and Purification of Esters.—The esters were prepared by Fischer's method from pure materials. After purification in the usual way, they were carefully fractionated. Kahlbaum's esters were simply fractionated.

Phenol.—The best obtainable phenol was dried in a vacuum desiccator over sulphuric acid for several days, and it then distilled at a constant temperature.

Ester Solutions.—Purified ester was weighed out and diluted with the specially purified alcohol. The amount of water required was added at this stage, and the whole solution was diluted with absolute alcohol to make the N-solution. Thus for a reaction mixture to be $N/2$ with regard to both phenoxide and ester and to contain 5% of water by volume, the ester solution would be made N and would contain 10% by volume of water.

The reaction was found to proceed with suitable velocity at 70° and with potassium phenoxide and ethyl acetate concentrations of

about $N/2$. Equal volumes (5 c.c.) of phenoxide and ester solutions were mixed in Jena glass tubes of about 13 or 14 c.c. capacity; these were then well corked and placed in the thermostat. Tubes were withdrawn at intervals, emptied into a beaker, rinsed with alcohol, and the liquid was titrated with standard acid. Some difficulty was found in obtaining an indicator giving a sharp end-point in phenolic solutions. Phenolphthalein and methyl-orange were valueless, but litmus and *p*-nitrophenol were the most satisfactory.

The following two tables show the velocity coefficients calculated from equation (6). The ethyl acetate and phenoxide were of equivalent strengths and the solutions contained 5% of water and no added water, respectively.

$a = c = 500$; $b = 2777{\cdot}7$.

t.	C.c. $N/2$-HCl.	x.	$a - x$.	$b - x$.	$kK \times 10^4$.
0	20	0	500·0	2777·7	—
10	15·6	110·0	390·0	2667·7	1·24
17	14·6	135·0	365·0	2642·7	1·21
25	13·6	160·0	340·0	2617·7	1·27
37	12·7	182·5	317·5	2595·2	1·19
50	11·2	202·5	297·5	2575·2	1·22
64	11·2	220·0	280·0	2557·7	1·23
112	9·7	257·5	242·5	2520·2	1·15
					Mean 1·22

$a = c = 500$; b (calc.) $= 83{\cdot}3$.

t.	Titre.	x.	$a - x$.	$b - x$.	$kK \times 10^4$.
0	17·3	0	432·5	83·3	—
10	16·5	20·0	412·5	63·3	2·11
15	16·3	25·0	407·5	58·3	2·16
25	16·1	30·0	402·5	53·3	2·44
45	15·7	40·0	392·5	43·3	2·07
					Mean 2·19

The following table summarises the results of these and six other experiments and exhibits the effects of varying the initial concentrations of ethyl acetate, water, phenoxide, and phenol:

a.	b.	c.	d.	$kK \times 10^4$ (range).	$kK \times 10^4$ (mean).
500	2777·7	500	—	1·15—1·27	1·22
500	83·3	500	—	2·07—2·44	2·19
500	2777·7	122·5	—	0·92—1·12	1·02
500	2777·7	247·5	—	1·01—1·16	1·05
1000	2777·7	487·5	—	0·96—1·15	1·05
250	2777·7	487·5	—	0·88—1·19	1·00
487·5	2777·7	487·5	532·0	1·30—1·41	1·34
487·5	2777·7	487·5	212·7	1·12—1·50	1·38

Summary.

1. In alcoholic solution, the reaction between phenoxides and the esters studied does not follow the usual bimolecular law.

2. Normally the reaction does not go to completion, and the time–titration curves suggest an equilibrium reaction.

3. There is no evidence to show that the reaction proceeds according to the equation

$$C_6H_5{\cdot}OK + CH_3{\cdot}CO_2C_2H_5 \longrightarrow C_6H_5{\cdot}O{\cdot}C_2H_5 + CH_3{\cdot}CO_2K.$$

4. There is also no evidence in favour of the view that the reaction proceeds as a result of " alcoholysis " of the phenoxide.

5. The reaction proceeds as a result of hydrolysis of the phenoxide by water present in, or added to, the solution.

6. A mathematical expression has been deduced for the reaction and the velocity coefficients are shown to be satisfactory.

In conclusion, I should like to thank Dr. J. C. Crocker, for suggesting the research and for his unfailing interest in it, also the Department of Scientific and Industrial Research for a grant which made it possible for the work to be undertaken.

CHELSEA POLYTECHNIC, S.W. [*Received, May 31st*, 1926.]

CCCXXVIII.—*Alternation in the Heats of Crystallisation of the Normal Monobasic Fatty Acids. Part II.*

By W. E. GARNER, F. C. MADDEN, and J. E. RUSHBROOKE.

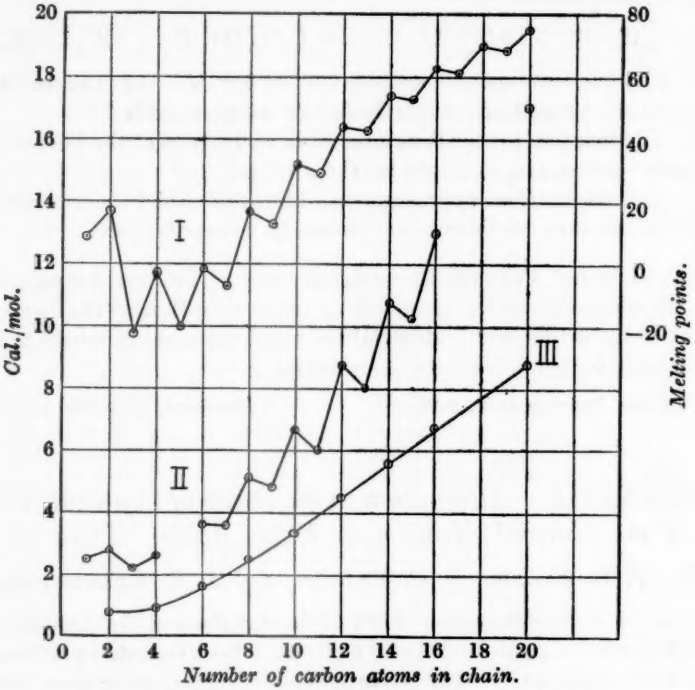
THE heats of crystallisation of five of the members of the homologous series of normal monobasic fatty acids have been reported previously (J., 1924, **125**, 881). The investigation of this homologous series has now been extended and the heats of crystallisation of seven more acids have been established. With the exception of stearic acid, the heats of all the even acids up to C_{20} are now known, and of the odd acids there are but three missing over this range.

The data which are available both from our own experiments and those of others are summarised in Table I and in the figure. It will be seen that the alternation in the heats of crystallisation (curve II) is as definite as for the melting points (curve I), but that it is essentially different in character. The melting-point curves of the odd and even members converge and approach a maximum value as the length of the carbon chain increases, whereas the curves for the heats of crystallisation diverge up to the tenth member and then take a parallel course. The heats of crystallisation are linear above decoic acid and for the higher members they are given by

$$Q = -3{\cdot}61 + 1{\cdot}030n \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where n is the number of carbon atoms in the chain. The linear

relationship between Q and n is evident from the differences ΔQ in Table I. Above C_{10} these differences are constant within experimental error.



I *Melting points.* II *Heats of crystallisation.* III Q/T.

TABLE I.

No. of C atoms and setting point (Abs. Temp.).		Heat of crystallisation, Q (Cal./mol.).		ΔQ for $2CH_2$.	
Odd.	Even.	Odd.	Even.	Odd.	Even.
1 (281·5)	2 (289·5)	2·52*	2·77*		
3 (251)	4 (270)	2·26†	2·64‡	−0·26	−0·13
5 (253)	6 (271·5)	—	3·60	—	0·96
7 (261·75)	8 (289·5)	3·58	5·11	—	1·51
9 (285·5)	10 (304·5)	4·85	6·69	1·27	1·58
11 (301·5)	12 (316·8)	5·99	8·75	1·14	2·06
13 (314·7)	14 (326·7)	8·02	10·74	2·03	1·99
15 (325·5)	16 (335·8)	10·30	12·98	2·28	2·24
17 (334·5)	18 (343·75)	—	—	—	1·98
19 (342·5)	20 (349·5)	—	16·95	—	1·98

* Landolt-Börnstein, Tabellen, 1912, IV, p. 830.

† Massol and Faucon (from equation, $M(l+s)/T = 30$); *Compt. rend.*, 1909, **149**, 345.

‡ Parks and Anderson (*J. Amer. Chem. Soc.*, **1926**, **48**, 1506).

The increment in the heat of crystallisation of the odd members on adding two methylene groups to the chain approaches the same constant value as is found for the even acids. From this it may be inferred that the packing of the methylene groups in the crystalline state is the same for the odd as for the even members. The suggestion that this was the case was made in the previous paper (*loc. cit.*, p. 885) and was supported by measurements on the molecular volumes of these acids in the solid state (Garner and Ryder, J., 1925, **127**, 720). The alternations in Q can therefore only be ascribed to an alternation in the arrangement of the terminal groups * as we pass from member to member.

In curve III, Q/T is plotted against n for the even acids (T in °Abs). This is linear above C_{10} and nearly so down to C_6. For the acids above decoic the following equation holds :

$$Q/T = -0{\cdot}0043 + 0{\cdot}002652n \quad . \quad . \quad . \quad . \quad (2)$$

where the coefficients have been calculated by the method of least squares. Combining (1) and (2) one obtains

$$T = (1{\cdot}030n - 3{\cdot}61)/(0{\cdot}002652n - 0{\cdot}0043) \quad . \quad . \quad (3)$$

as the equation for the melting-point curve of the even acids above decoic. From this equation, the melting-point curve should reach its maximum value at 115°. A similar value may be calculated for the odd acids, but as these crystallise in two forms, the determination of the heat of crystallisation of the form stable at the melting point is more difficult than for the even acids, and the values of Q are less accurate.

Equation (3) assumes that the linear relationships for Q and Q/T persist up to $n = \infty$; very strong arguments must be forthcoming before such assumptions are worthy of serious consideration, especially in the case of Q/T. The arguments which can be adduced in support are of a twofold character : (*a*) those based on the experimental results obtained on the melting points and heats of combustion of the normal dibasic fatty acids, and (*b*) a theoretical deduction of the relationship between the heat of crystallisation and melting point, based on statistical laws.

The Dibasic Fatty Acids.—The melting points of the even acids in this homologous series decrease and those of the odd acids increase with lengthening of the carbon chain. The melting-point curves converge so rapidly that by $n = 30$ the temperatures for the odd and even acids are identical within 2 or 3°. From the values given in Beilstein, the convergence temperature is approximately 118°, and from the results of Fairweather (*Phil. Mag.*, 1926, **1**, 944) on the even members, 123°. These values are as near to that of the

* See subsequent note.

convergence temperature of the monobasic acids as can be expected in view of experimental errors in the coefficients of equation (3).

For molecules of straight-chain compounds in which n approaches infinity, the effect of the terminal groups becomes negligible, and the physical properties of the crystal will be mainly determined by the hydrocarbon chain. Hence the agreement between the convergence temperatures mentioned above can have no other meaning than that the packing of the hydrocarbon chain in the mono- and di-basic acids is the same. This conclusion is supported by the work of Verkade, Hartmann, and Coops (*Proc. K. Akad. Wetensch. Amsterdam*, 1924, **27**, 859), who have measured the heats of combustion of the members of the dibasic acids with 2 to 12 carbon atoms. The difference between the heat of combustion of an odd acid and the mean of those for the next lower and higher acids is given below:

2		4		6		8		10		12	
	3		5		7		9		11		
Diff.	−2·15		+1·85		+1·50		+1·35		+1·60		Cal./mol.

Excluding the first difference, the mean is 1·58 * Cal./mol. This should also be the difference between the mean heat of crystallisation of two adjacent even acids and that for the intermediate odd acid. These have not been determined for the dibasic acids but are available for the monobasic acids:

6		8		10		12		14		16	
	7		9		11		13		15		
Diff.	0·78		1·05		1·73		1·73		1·56		Cal./mol.

The mean of the last three is 1·67 Cal./mol.* The two means are in agreement within experimental error. These facts are suggestive: the differences between the odd and even mono- and di-basic acids very probably have a similar physical origin; therefore there is every reason to expect that the convergence temperatures for the two homologous series will be identical.

Kinetic Theory of Melting of Members of an Homologous Series.

The general character of the structure of the crystals of straight-chain compounds has been made manifest by the X-ray method of

* It is of interest to note that these differences are equal in magnitude to the heat liberated on sublimation of a methylene group (see Smiles, "Physical Properties and Chemical Constitution," 1910, for the heat of evaporation from the liquid state). If one of the methylene groups in the crystal molecules of the odd acids is in a state analogous to the gaseous state, *i.e.*, is not within the sphere of influence of adjacent hydrocarbon chains, then during crystallisation the group in question undergoes changes analogous to those occurring during evaporation from the liquid state. Its heat of crystallisation is thus negative and about 0·6 Cal./mol.

analysis (Müller and Shearer, J., 1923, **123**, 2043, 3152, 3156). The molecules of these compounds are arranged in straight chains with their methylene groups placed alternately on opposite sides of the chains. Contact between the molecules is made through the methylene and terminal groups. On the faces of the crystal, the molecules are attached by $\frac{1}{2}(n-2)$ methylene groups and the two terminal groups. In the process of melting the conjoined groups separate and the molecule enters the liquid state; on solidification, the reverse change occurs. A consideration of the kinetics of these processes may serve to elucidate some of the problems which arise in the study of the melting points of homologous series and other organic compounds.

On account of the rotation which can occur at the carbon–carbon linking, a molecule which is attached to the surface at a number of points may leave it in stages, in each of which one point of attachment is broken at a time. In the case of a straight-chain compound, the methylene groups in the middle of the chain being immovable when the ends of the chain are fixed, a molecule must leave the surface beginning at a terminal group and progressively untwisting itself until it is finally completely detached. We have thus to take into account in the case of a single molecule a succession of processes of which the probabilities will be given by equations of the type $P = ke^{-q/KT}$, where q is the energy of activation in ergs per molecule, k is a constant,* K the Boltzmann constant, and T the absolute temperature.

It can be readily shown that the probability P' that a molecule will leave the solid surface is given by

$$P' = k_1'^{\frac{1}{2}(n-2)} \cdot k_2' \cdot k_3' e^{-\{\frac{1}{2}(n-2)q_1' + q_2' + q_3'\}/KT} \quad . \quad . \quad (4)$$

where q_1', q_2', and q_3' are the energies of activation in ergs per molecule for methylene, methyl, and carboxyl groups, respectively, and k_1', k_2', and k_3' are corresponding constants dependent on spatial considerations, times of relaxation, etc., about which very little is known.

Also, the probability that a molecule near a crystal face will leave the liquid state is given by a similar equation

$$P'' = k_1''^{\frac{1}{2}(n-2)} \cdot k_2'' \cdot k_3'' \cdot e^{-\{\frac{1}{2}(n-2)q_1'' + q_2'' + q_3''\}/KT} \cdot \left[\frac{x}{x+(n-2)y+z}\right] \quad (5)$$

where q_1'', q_2'', q_3'' are the energies of activation, etc., $x/[x + (n-2)y + z]$ is a factor which has been introduced to allow for the fact that the longer the carbon chain the smaller the probability

* The nature of k has been discussed previously for homogeneous reactions (*Phil. Mag.*, 1925, **49**, 463).

that an activated terminal group will collide with the surface in the right place; x and z are the areas of the terminal groups exposed on the face of the crystal, and y is the area of the methylene group. Approximately, $x = y = z$, and the factor becomes $1/n$. At the melting point, $P' = P''$, therefore

$$(k_1'/k_1'')^{\frac{1}{2}(n-2)} . (k_2'/k_2'')(k_3'/k_3'') . n = e^{-\{\frac{1}{2}(n-2)q_1+q_2+q_3\}/KT} \quad . \quad (6)$$

where $q_1 = q_1'' - q_1'$, etc. A similar equation [(7), not given] holds for the member with $n + 2$ carbon atoms. On dividing (7) by (6) and assuming a constancy of k_1', k_2', k_3', etc. with increase in temperature, we obtain

$$\log_e \{k_1'(n + 2)/k_1''n\} = q_{n+2}/KT_{n+2} - q_n/KT_n$$

where q_{n+2} and q_n are the heats of crystallisation per molecule of the $(n + 2)$th and nth members of the homologous series. T_{n+2} and T_n are the melting points.

For a gram-molecule,

$$\log_{10}\{k_1'(n + 2)/k_1''n\} = Q_{n+2}/4{\cdot}57T_{n+2} - Q_n/4{\cdot}57T_n = 5{\cdot}30/4{\cdot}57 = 1{\cdot}15 \quad . \quad . \quad (8)$$

For members above C_{10}, $\log(n + 2)/n$ is small compared with $\Delta Q/T$ for two adjacent even members, and when n is large

$$\Delta(Q/4{\cdot}57T) = \log_{10} k_1'/k_1''.$$

k_1' is dependent on the time which elapses between the activation of a methylene group on the surface and its detachment. Since this time is determined by intramolecular changes, k_1' should be independent of temperature. k_1'' is a similar factor for the processes occurring on crystallisation. In the analogous processes occurring in chemical change, the logarithms of factors of a similar nature to the above are constant over a range of temperature of 100° within experimental error. There is thus every reason to expect $\log k_1'/k_1''$ to be constant on theoretical grounds and this view is supported by the constancy of $\Delta(Q/4{\cdot}57T)$ found for the acids C_{10} to C_{20}.

The Lower Members of Homologous Series.

The departure from the linear relationships (1) and (2) in the cases of the lower members (see figure) is an indication of an important physical difference between the higher and the lower members in either the liquid or the solid states. This physical difference *gradually* disappears as the series is ascended. An examination of a number of physical properties for the series of monobasic acids, *e.g.*, the specific heats and specific volumes in the liquid state, the volume of the crystal, length of crystal molecule from *X*-ray

measurements,* etc., fails to reveal the nature of this physical difference.

From the heats of crystallisation in Table I some light can be thrown on the matter. The heat of crystallisation of the methylene group is 1·030 Cal. for the acids above C_{10}. Assuming this to be constant even for the lower members, the heats of crystallisation of the terminal groups may be calculated. They change from + 2·77 for C_2 up to − 1·55 for the higher members :

C_2.	C_4.	C_6.	C_8.	C_{10}.	C_{12}.	C_{14}.	C_{16}.	C_{20}.
+2·77	+0·58	−0·52	−1·07	−1·55	−1·55	−1·62	−1·44	−1·59

From a study of a solid model, in the construction of which Bragg's dimensions for carbon, hydrogen, and oxygen atoms, and Müller and Shearer's structure for the fatty acids are assumed, a physical interpretation of the above change can be given. It is found that the area of the cross-section of the crystal cell of the higher acids is determined entirely by the methylene groups and that the methyl and carboxyl groups † can rotate freely within the crystal without touching adjacent molecules. The empty spaces between the adjacent methyl and carboxyl groups of neighbouring molecules disappear on liquefaction, for all of the groups can come into contact in the liquid state. The increase in the density of packing of these groups which occurs on liquefaction would account for the negative heat of crystallisation in the higher members.

In crystals of acetic acid, where there are no methylene groups, the terminal groups must be in contact and hence possess a positive heat of crystallisation. Judging from the above values, as more and more methylene groups are introduced into the molecule, the terminal groups are forced farther and farther apart, their heat of crystallisation changes sign, and finally a constant negative value is attained.

In terms of equation (6), we are no longer justified in assuming that the values of k_2 and k_3 for the terminal groups are constant for the lower members, hence equation (8) no longer represents the facts, but the above interpretation cannot readily be formulated mathematically.

No further light has been thrown on the β-odd acids. Indeed, as the following scheme shows, there is some disturbing factor operating

Heat of α—β transition for odd acids.

	9	11	13	15	
$Q_{\alpha-\beta}$	1·37	1·84	0·94	1·20	Cal./mol.

* This has not been determined accurately for the lower acids.

† For structure of carboxyl group, see Garner and Ryder (*loc. cit.*).

during the α—β change which does not affect the change from the liquid to the α-form. The deviations are outside the experimental error. The heat of transition of C_{11} has been redetermined in a new apparatus, and the previously published value confirmed. It is possible that the β-form is a mixture of two modifications which occur in inner equilibrium with one another in the solid state. It has been observed that when a trace of water is present in an odd acid the transition α—β occurs with a marked swelling of the solid which very frequently is accompanied by a rupture of the container. The density of the β-form is, however, greater than that of the α-form. In the absence of water, the change from one form to the other is much less evident. This question calls for further investigation, for the work of Smits suggests the possibility that the transition would not occur if the acids were very carefully dried.

On the basis of the above considerations, we venture to put forward two hypotheses: (1) *the convergence temperature of all homologous series lies in the neighbourhood of* 120°; and (2) *the melting-point curve of the higher members of any homologous series is given by the relationship* $T = (x + 1{\cdot}030n)/(y + 0{\cdot}00265n)$, where x and y are coefficients depending on the terminal groups.

Experimental.

A number of the monobasic acids were obtained from Kahlbaum, *e.g.*, C_6, C_7, C_{14}, and C_{16}, and others, C_{13}, C_{15}, and C_{17}, from the Eastman Kodak Co. These acids were not quite pure, melting, as a rule, 2—3° below the correct m. p. They were purified by distillation or crystallisation until a constant setting point was obtained. The specimen of eicosoic acid was kindly lent to us by Mr. N. K. Adam.

The details of the experimental technique have been described previously. Two calorimeters were used; one was constructed by Mr. Rushbrooke for the determination of the heats of crystallisation of about 5 g. of material, and had a water-equivalent of 345·3; this was used for C_{13}, C_{14}, C_{15}, and C_{20} acids. The other had been used previously by Garner and Randall (*loc. cit.*). The water-equivalent of this calorimeter was now found to be 691·4, in agreement with the previous value of 690·5.

The specific heat of the glass forming the container was determined for two new ranges of temperature. The values for all the ranges are given in Table II.

Table II.

Temp.	20—100°	19—77°	19—44°	18—0°	18——13°	18——35°
Sp. heat.	0·2005	0·1962	0·1878	0·1835	0·1803	0·1799

The mean specific heat of nickel between −33° and 20° was

found to be 0·1001; for other ranges of temperature the values of Schlett (Tabellen) were taken.

The same methods of calculation of the specific heats and heats of crystallisation were adopted as described previously, except that for C_{13} and C_{15} acids a graphical method was employed as well. The experimental data are recorded in Tables III—X. In the majority of cases, the means of duplicate experiments are given. The degree of reproducibility of results was of the same order as in the previous investigation (*loc. cit.*), where individual experimental results are given.

TABLE III.

(*Caproic acid: setting point*, — 3·6°).

Exp. No.	Temp. range.	Weight of Acid.	Glass.	Platinum.	Nickel.	Fall in temp.	Rise in temp.
1—3	0—23°	7·6714	4·5256	0·2524	1·8985	22·53°	$0·161_3$°
4—6	−10—19	,,	,,	,,	,,	28·30	$0·543_0$
7—9	−33—18·5	,,	,,	,,	,,	51·70	$0·694_3$

I. From 1, 2, and 3, $\sigma_l = 0·5105$.
II. From 4 to 9, and I, $\sigma_s = 0·4495$; $Q = 31·15$ cal./g.

TABLE IV.

(*Heptoic acid: setting point*, −7·5°).

Exp. No.	Temp. range.	Weight of Acid.	Glass.	Platinum.	Nickel.	Fall in temp.	Rise in temp.
1—3	0—20°	11·6806	4·6955	0·266	2·401	20·86°	$0·207_0$°
4—6	30—20	,,	,,	,,	,,	9·73	$0·097_7$
7	−15—20	,,	,,	,,	,,	34·49	0·800
8						39·97	0·857
9						35·95	0·824
10	−35—19	11·8990	5·9224	0·266	1·8982	56·66	1·040
11						49·65	0·981
12						55·04	1·024

I. From 1 to 6, $\sigma_l = 0·4928$.
II. From 7 to 12, and I, $\sigma_s = 0·4752$; $Q = 27·50$ cal./g.

TABLE V.

(*Nonoic acid: setting point*, 12·35°).

Exp. No.	Temp. range.	Weight of materials.	Fall in temp.	Rise in temp.
1	−33—16°	As in previous paper.	49·58°	0·963°
2	−42—16		58·86	1·0265

Combining these results with those of Garner and Randall (*loc. cit.*), $\sigma_\beta = 0·3653$; $Q = 39·29$ cal./g.

TABLE VI.

(*Tridecoic acid: setting point*, 41·1°).

Weight of			
Acid.	Glass.	Platinum.	Nickel.
8·7132	6·4994	0·2008	2·9781

No. of exp.	Range of temp.	Fall in temp.	Rise in temp.	No. of exp.	Range of temp.	Fall in temp.	Rise in temp.
1—3	0—18°	17·47°	$0·259_7$°	8	34—17°	17·52°	0·384°
4	26—17	10·02	0·160	9	36—17	18·86	0·405
5	28—17	11·93	0·191	10	38—17	21·28	0·460
6	30—17	13·25	0·276	11—13	44—17	25·66	$1·467_7$
7	32—17	15·59	0·342	14—16	76—17	58·79	$2·085_3$

By a graphical method one obtains

$Q_\alpha = 37·43$ cal./g.; $Q_\beta = 41·81$ cal./g.; $\sigma_l = 0·5456$ cal./deg.;
$\sigma_\alpha = 0·4307$ cal./deg.; $\sigma_\beta = 0·4322$ cal./deg.

TABLE VII.

(*Myristic acid: setting point*, 53·7°).

Weight of			
Acid.	Glass.	Platinum.	Nickel.
6·4092	4·1884	0·2008	3·0904

No. of exp.	Range of temp.	Fall in temp.	Rise in temp.	No. of exp.	Range of temp.	Fall in temp.	Rise in temp.
1—7	43—24°	19·24°	$0·248_4$°	12—19	84—23°	62·01°	$1·682_8$°
8—11	57—24	32·93	$1·300_5$				

I. From 1 to 7, $\sigma_s = 0·5209$ cal./deg.
II. From 8 to 19, and I, $\sigma_l = 0·5157$; $Q = 47·07$ cal./g.

TABLE VIII.

(*Pentadecoic acid: setting point*, 52·1°).

Weight of			
Acid.	Glass.	Platinum.	Nickel.
10·3201	6·4279	0·2008	3·9136

No. of exp.	Range of temp.	Fall in temp.	Rise in temp.	No. of exp.	Range of temp.	Fall in temp.	Rise in temp.
1—2	30—20°	8·13°	0·161°	29—30	42—20°	19·37°	$0·504_5$°
3—7	32—20	9·30	$0·169_4$	31—35	45—20	22·04	0·592
8—9	33·5—20	11·20	0·238	36—37	47—20	24·53	0·671
10—11	36—20	13·42	0·317	38—39	49—20	25·77	1·087
12—18	38—20	15·59	$0·430_6$	40—41	50—20	26·70	1·314
19—20	40—20	16·10	$0·451_5$	42—45	55—20	31·94	$2·027_0$
21—28	41—20	18·21	$0·486_8$	46—49	88—20	61·52	$2·656_0$

$Q_\alpha = 42·47$ cal./g.; $Q_\beta = 47·40$ cal./g.; $\sigma_l = 0·5316$ cal./deg.;
$\sigma_\alpha = 0·4668$ cal./deg.; $\sigma_\beta = 0·4603$ cal./deg.

TABLE IX.

(Palmitic acid: setting point, 62·3°).

Exp. No.	Temp. range.	Weight of Acid.	Glass.	Platinum.	Nickel.	Fall in temp.	Rise in temp.
1—3	22—100°	12·5535	6·2055	0·266	1·8990	77·01°	$1·803_0$°
4—5	22— 68	,,	,,	,,	,,	46·40	1·438
6	22— 66	,,	,,	,,	,,	44·48	1·405
7—9	22— 56	,,	,,	,,	,,	34·03	$0·393_6$
10—12	22— 53	,,	,,	,,	,,	33·50	$0·367_3$

I. From 10 to 12, $\sigma_s = 0·4920$.

II. From 4 to 6, 10 to 12, and I, $\sigma_l = 0·5416$; $Q = 50·59$ cal./g.

[Mrs. Stratton and Partington (*Phil. Mag.*, 1924, **48**, 1085), working with very carefully purified palmitic acid (setting point 62·65°), by electrical heating at the melting point obtained $Q = 51·03$ cal./g.]

TABLE X.

(Eicosoic acid: setting point, 74·2°).

Exp. No.	Temp. range.	Weight of Acid.	Glass.	Platinum.	Nickel.	Fall in temp.	Rise in temp.
1—3	56—20°	10·3867	4·7523	0·2008	2·5944	32·65°	$0·563_7$°
4—6	66—20	,,	,,	,,	,,	42·43	$0·756_7$
7—9	77—20	,,	,,	,,	,,	51·97	$2·568_3$
10—12	100—20	,,	,,	,,	,,	74·21	$3·030_7$

I. From 1 to 3, $\sigma_s = 0·4597$ cal./deg.

II. From 4 to 6, $\sigma_s = 0·4772$ cal./deg.

III. From 7 to 12, and II, $\sigma_l = 0·5663$ cal./deg.; $Q = 54·24$ cal./g.

TABLE XI.

Mean specific heat in liquid state.

6	7	8	9	10	11	12	13	14	15	16	20
0·51	0·49	0·51	0·50	0·50	0·52	0·51	0·55	0·52	0·53	0·54	0·57

The mean specific heats of the acids in the liquid state over a temperature range of approximately 30° just above the melting point show no evidence of the presence of alternation; there is a slight rise in specific heat as the series is ascended.

The average mean specific heat of the solid form stable at the melting point is 0·46, somewhat lower than the mean for the liquid acids. It was not convenient to measure these over comparable ranges of temperature. Thus it is impossible to draw any conclusions as to the presence or absence of alternation in the mean specific heats of the solids.

Summary.

The heats of crystallisation of caproic, heptoic, tridecoic, myristic, pentadecoic, palmitic, and eicosoic acids have been determined.

These values, together with those previously published, show a very marked alternation as the series of acids is ascended.

Above decoic acid, the heat of crystallisation of the even acids is given by the equation $Q = -3{\cdot}61 + 1{\cdot}030\,n$, where n is the number of carbon atoms in the chain, and the melting points of these acids are given by $T = (-3{\cdot}61 + 1{\cdot}030n)/(-0{\cdot}0043 + 0{\cdot}002652n)$. This equation has been shown to have a statistical basis.

Similar equations have been obtained for the odd acids, and the conclusion is drawn that the arrangement of the methylene groups is the same for both the even and the odd acids in the solid state.

The convergence temperature for the monobasic acids is 115°, in agreement with that for the dibasic acids.

The heat of crystallisation of the terminal methyl and carboxyl groups changes from a positive to a negative value as the number of carbon atoms changes from 2 to 10.

The heat of transition of the α- to the β-form of the odd acids is erratic owing to the presence of a disturbing factor, very possibly water.

There is no alternation in the specific heats of the acids in the liquid state.

We wish to express our thanks to the Chemical Society for a grant towards the cost of some of these acids, and to Mr. N. K. Adam for the loan of a specimen of eicosoic acid.

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CCCXXIX.—*The Tautomerism of Amidines. Part VI. Methylation of 4-Anilino-2-phenyl-6-methylpyrimidine.*

By ROBERT FORSYTH and FRANK LEE PYMAN.

IN previous parts of this series it has been shown that methylation of glyoxalines (wholly cyclic amidines) and of open-chain amidines, by methyl salts, yields mixtures of the isomeric *N*-methyl derivatives, in which the relative amounts of the two isomerides produced vary from case to case. In some cases, the amount of one of the isomerides produced is very small; for example, benzenylphenylamidine (I or II) gave phenylmethylamidobenzenylimidine (III) in 82·7% yield, and benzenylphenylmethylamidine (IV) in 0·55% yield (Pyman, J., 1923, **123**, 3359).

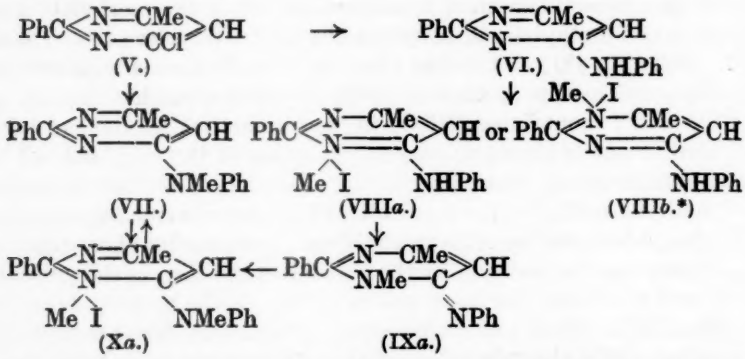
$CPh(:NPh)\cdot NH_2$ (I.) or $CPh(:NH)\cdot NHPh$ (II.) $\longrightarrow$
$CPh(:NH)\cdot NMePh$ (III.) and $CPh(:NMe)\cdot NHPh$ (IV.)

Here the formation of (IV) had escaped the notice of von Pechmann (*Ber.*, 1897, **30**, 1782), who regarded (III) as the sole product of the methylation of (I) or (II). In other cases also, one of us was able to show that the supposed homogeneous methylation of open-chain amidines was incorrect.

It seemed to us, therefore, of interest to re-examine some of the cases of alleged homogeneous methylation of partly cyclic amidines, and this paper deals with a re-investigation of the methylation of 2-phenyl-6-methyl-4-anilinopyrimidine (VI). Wheeler (*Amer. Chem. J.*, 1898, **20**, 481) states that when this base is heated with methyl iodide and methyl alcohol at 100°, it yields a methiodide (m. p. 210—213°; containing $2H_2O$) in which methyl iodide has been added to one of the tertiary nitrogen atoms of the ring, and not to the anilino-group, since this salt yields with alkali not 2-phenyl-6-methyl-4-methylanilinopyrimidine (VII), but the starting material, 2-phenyl-6-methyl-4-anilinopyrimidine. Our results show that on carrying out the reaction by the above method, *i.e.*, in the presence of methyl alcohol, the main product (79%) is the hydriodide (m. p. 238—239°; anhyd.) of unchanged 2-phenyl-6-methyl-4-anilinopyrimidine, whilst the only other product which could be isolated (yield 15%) was a methiodide, m. p. 220°, containing $2H_2O$. This separated first and is presumably identical with Wheeler's salt. On treatment with alkali, however, it does not give the original anilinopyrimidine, but loses hydriodic acid, giving a base, m. p. 193—194°, which is a methyl homologue of the anilinopyrimidine. Wheeler's recovery of the anilino-base is clearly due to the presence of its hydriodide in the product which he basified. Since the formation of the iodide of the original base was presumably due to the removal of hydriodic acid from methyl iodide and methyl alcohol, with the formation of dimethyl ether, we next heated the base with methyl iodide in the absence of methyl alcohol, and in this case obtained the methiodide, m. p. 220°, as the main product (77%), accompanied by a quantity of the starting material (11%) and an iodide B, m. p. 182—183° (7·1%). No other product could be isolated from the mixture.

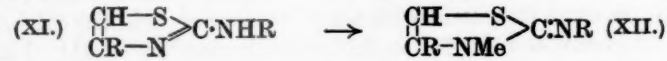
The methiodide, m. p. 220°, which is colourless, must be either 2-phenyl-3 : 6 (or 1 : 6)-dimethyl-4-anilinopyrimidinium iodide (VIII, *a* or *b*), since on treatment with alkali it does not yield the colourless base 2-phenyl-6-methyl-4-methylanilinopyrimidine (VII), but a yellow, unstable base (m. p. 193—194°) which must be either 4-*phenylimino*-2-*phenyl*-3 : 6-*dimethyl*-3 : 4-*dihydropyrimidine* (IX*a*) or 4-*phenylimino*-2-*phenyl*-1 : 6-*dimethyl*-1 : 4-*dihydropyrimidine* (IX*b*). Further methylation of this product with methyl iodide yields a salt identical with the methylation product of 2-phenyl-6-

methyl-4-methylanilinopyrimidine; it must therefore be 4-*methylanilino*-2-*phenyl*-3 : 6 (or 1 : 6)-*dimethylpyrimidinium iodide* (X, *a* or *b*). The *iodide B* (m. p. 182—183°) proved to be a molecular compound of the quaternary iodide (X, *a* or *b*) with the original base (VI), and thus, whilst 95·1% of the material has been accounted for, no evidence of the formation of the methylanilino-base (VII) has been obtained.



It is interesting to note that the quaternary salt (X, *a* or *b*) loses methyl iodide on distillation, and yields the methylanilino-base (VII), that is the *N*-methyl derivative which is produced only in small quantity, if at all, on the methylation of (VI). This behaviour is similar to that of the methiodides of *N*-methyl-4(5)-nitro-(and bromo-) glyoxalines (J., 1925, **127**, 573, 1832). These also yield on distillation those tertiary bases which are produced in inferior quantity by methylation of the parent glyoxalines by methyl salts.

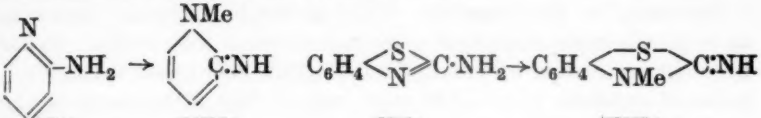
The formation of (VIII, *a* or *b*) as the main (or possibly sole) product of methylation of (VI) by methyl iodide falls into line with numerous other results of alkylation by methyl salts of those partly cyclic amidines which contain one of their nitrogen atoms as a member of an aromatic nucleus. Thus, the 2-amino-, -alkylamino-, and -anilino-thiazoles (XI) yield as main products the 3-methyl derivatives (XII) (Young and Crookes, J., 1906, **89**, 59; and previous investigators), and in these cases the isomerides methylated on the amino-group were not isolated; 2-aminopyridine (XIII) gives



1-methylpyridon-2-imide (XIV) with but little 2-methylaminopyridine (Tschitschibabin and Konowalowa, *Ber.*, 1921, **54**, 814);

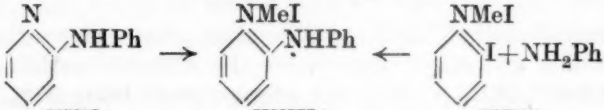
* Adoption of the formula (VIII*b*) would lead to corresponding formulæ (IX*b*) and (X*b*) with methyl attached to the 1- in place of the 3-nitrogen atom.

and 1-aminobenzthiazole (XV) gives 1-imino-2-methyl-1 : 2-dihydrobenzthiazole (XVI) with probably some 1-methylaminobenzthiazole (Hunter, this vol., p. 1385).



(XIII.) (XIV.) (XV.) (XVI.)

The main product in each case is the substance methylated on the ring nitrogen atom. The cause of this fact seems to us to lie in the structure of the molecule rather than in the relative basicity of the two nitrogen atoms. The latter explanation, which has been advanced by several previous investigators (for references, see Pyman, J., 1923, **123**, 367) to explain the results of methylating open-chain and partly cyclic amidines, seems to us unsatisfactory. It is true that in the methylation of open-chain amidines, when nitrogen atoms attached to aryl and alkyl groups are in competition, the main products are those in which the methyl group has attached itself to the arylamino-nitrogen atom, but this may be due, not to the feebler basicity of the arylamino-group, but to a tendency of the aryl group to attract the double linking into the αβ-position; thus the predominant formation of (III) on the methylation of (I) or (II) may be attributed to the reaction of this compound mainly in the form (I). The argument that the methylanilino-compounds are the main products because aniline is less basic than alkylamines is countered by the facts that whilst the bases $NMePh{\cdot}CPh{:}NR$ ($R = H$, CH_2Ph, Me) are the main products of methylation of $NPh{:}CPh{\cdot}NHR$ or $NHPh{\cdot}CPh{:}NR$, proportions of the isomerides $NPh{:}CPh{\cdot}NMeR$ are produced which increase with the basicity of $R{\cdot}NH_2$, and further that in the methylation of $NMe{:}CPh{\cdot}NH_2$ or $NHMe{\cdot}CPh{:}NH$, the base $NMe_2{\cdot}CPh{:}NH$, in which the more strongly basic amino-residue had become methylated, was produced in larger quantity than $NHMe{\cdot}CPh{:}NMe$ (Pyman, *loc. cit.*). A further argument against this view is found in the result of methylation of 2-anilinopyridine (XVII) with methyl iodide, when 2-anilinopyridine methiodide (XVIII), identical with the product of interaction of 2-iodopyridine methiodide (XIX) with aniline, is obtained, apparently

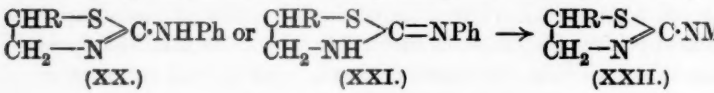


(XVII.) (XVIII.) (XIX.)

as the sole product (Steinhäuser and Diepolder, *J. pr. Chem.*, 1916, **93**, 387), for if the more feebly basic nitrogen atom had been

methylated preferentially, then 2-methylanilinopyridine should have been produced in greater quantity than (XVIII), since aniline ($K = 4{\cdot}6 \times 10^{-10}$) is a feebler base than pyridine ($K = 2{\cdot}4 \times 10^{-9}$).

Reference to the structure of the molecule, however, seems to us to give a more consistent systematisation of the results. It has been shown (compare Pyman, J., 1923, **123**, 3359) that the methylation of amidines by methyl salts leads to the attachment of the methyl group to the doubly-linked nitrogen atom in the case of open-chain and wholly cyclic amidines, and the methylation of (IX, *a* or *b*), resulting in the formation of (X, *a* or *b*) extends these proofs to a case of a partly cyclic amidine. It appears, then, that the reason why those partly cyclic amidines which contain one of their nitrogen atoms as a member of an aromatic nucleus yield with methyl salts mainly the isomerides methylated on the ring nitrogen atom, is because they tend to react mainly in the form in which the ring nitrogen atom is doubly-linked, that is, as amino-derivatives of aromatic compounds rather than as the isomeric iminodihydro-derivatives. Thus, for example, we attribute the formation of (XVI) as the main product of the methylation of 1-aminobenzthiazole to the reaction of this substance according to formula (XV) and not in the iminodihydro-form as Hunter (*loc. cit.*) believes. The common behaviour of the partly cyclic amidines derived from pyridine, pyrimidine, thiazole, and benzthiazole in yielding on methylation with methyl salts mainly compounds methylated on the ring nitrogen atom, no matter whether the side-chain nitrogen atom is present as an alkyl- or aryl-amino-group, is doubtless associated with their common feature, the aromatic character of their nuclei. Where, however, the ring is partly reduced and has lost its aromatic character, the phenyl group of an anilino-substituent can compete successfully for the proximity of the double linking, bringing it to the $\alpha\beta$-position, and thus the compounds (XX) or (XXI) yield as main products the substances (XXII), since they react mainly in the form (XXI) (Young and Crookes, *loc. cit.*).



EXPERIMENTAL.

2-Phenyl-6-methyl-4-hydroxypyrimidine was prepared from benzamidine and ethyl acetoacetate by Pinner's method ("Die Imidoäther," 1892, p. 240), the average yield being 97% of the theoretical of the pure compound, m. p. 223—225° (corr.) (Pinner gives m. p. 216°). From this, 2-phenyl-6-methyl-4-chloropyrimidine (V) was prepared either by the action of phosphorus pentachloride

(Pinner, *op. cit.*, p. 246) or of phosphorus oxychloride (Schmidt, *Ber.*, 1902, **35**, 1575). In each case, the crude product was purified from phosphorus compounds by crystallisation from ether (these separating first) and gave the pure substance, m. p. 71° as stated by previous authors, in yields of 88 and 85% respectively.

2-Phenyl-6-methyl-4-anilinopyrimidine (VI) was prepared by a modification of Pinner's method (*op. cit.*, p. 248). Aniline (2 mols.) was added to an ethereal solution of 2-phenyl-6-methyl-4-chloropyrimidine (1 mol.), and the ether distilled off. On heating the mixture to 100°, an exothermic reaction took place, and the product solidified. After basifying and removing excess of aniline by distillation with steam, the anilino-base separated and was recrystallised from alcohol, from which it separates in coarse, colourless, prismatic needles, m. p. 161—162° (corr.), in 97% yield. (Pinner gives m. p. 150—153°, Wheeler 160—161°.)

The hydrochloride separates from warm dilute hydrochloric acid as a gelatinous mass, but crystallises from alcohol in fine, colourless needles, m. p. 258—259° (corr.), which are anhydrous (Found: Cl, 12·1. Calc.: Cl, 11·9%). (Pinner and Wheeler both give m. p. 240°.)

The hydriodide crystallises from water or alcohol in fine, colourless needles, m. p. 238—239° (corr.), which are anhydrous and sparingly soluble in water, but more readily soluble in alcohol (Found: I, 32·9. Calc.: I, 32·7%). (Wheeler gives m. p. 231°.)

The nitrate crystallises from dilute nitric acid in rosettes of fine, opaque needles, containing $1H_2O$, which is lost in a vacuum over sulphuric acid (Found: loss, 4·9; N, 16·6. $C_{17}H_{15}N_3,HNO_3,H_2O$ requires H_2O, 5·3; N, 16·4%). The air-dried salt sinters at 95—100° and finally melts sharply at 155—156° (corr.). The vacuum-dried salt melts at 158—159° (corr.). (Pinner gives m. p. 85—87°.)

The *hydrogen oxalate* crystallises from a large volume of alcohol in fine, feathery needles, m. p. 242—243° (decomp.; corr.), which are anhydrous (Found: C, 64·9; H, 5·0. $C_{17}H_{15}N_3,C_2H_2O_4$ requires C, 64·9; H, 4·8%).

The *picrate* crystallises from alcohol in clusters of yellow, prismatic needles, m. p. 195—196° (decomp.; corr.) (Found: N, 16·8. $C_{17}H_{15}N_3,C_6H_3O_7N_3$ requires N, 17·1%).

Methylation.—(*A*) *In the presence of methyl alcohol.* 2-Phenyl-6-methyl-4-anilinopyrimidine (6·525 g.), methyl alcohol (6 c.c.), and methyl iodide (3 c.c.) were heated for 7 hours at 100°. On cooling, pale yellow needles (4·9 g.; m. p. 207—210°) separated, and further crops of crystalline hydriodides were obtained on concentration. After prolonged fractional crystallisation from alcohol, these gave first 2-phenyl-3 : 6 (or 1 : 6)-dimethyl-4-anilinopyrimidinium

iodide (1·677 g.; m. p. 216°), then 2-phenyl-6-methyl-4-anilinopyrimidine hydriodide [5·087 g.; m. p. 235—236° (corr.)], which did not depress the m. p. of a known specimen. The bases in the mother-liquors were worked up first as hydrogen oxalates, and then as picrates, further quantities of the salts of the starting material being obtained [0·796 g. of hydrogen oxalate, m. p. 241—242° (corr.), and 2·12 g. of picrate, m. p. 195°, both identified by the mixed m. p. method]. The yield of 2-phenyl-6-methyl-4-anilinopyrimidine recovered is thus 78·77% and that of the methylated product 15·28%, the total material recovered being 94·05%.

(*B*) *In the absence of methyl alcohol.* 2-Phenyl-6-methyl-4-anilinopyrimidine (26·1 g.) and methyl iodide (6·8 c.c.) were heated for 3 hours at 100°. Fractional crystallisation of the products from alcohol gave first 2-phenyl-3 : 6 (or 1 : 6)-dimethyl-4-anilinopyrimidinium iodide (m. p. 220°; yield 33·854 g., 77·1%) and then iodide B (m. p. 182—183°; yield 2·393 g., 7·37%). The mother-liquors were evaporated to dryness and extracted with ether, which removed unchanged 2-phenyl-6-methyl-4-anilinopyrimidine as base (m. p. 157—159°; yield 0·81 g., 3·1%). The material undissolved in ether was dissolved in water and basified, when 2·52 g. of base, m. p. 147—152°, were precipitated, and a small quantity of oily base was collected by means of ether. Both fractions were converted into picrates, and gave 2-phenyl-6-methyl-4-anilinopyrimidine picrate (m. p. 195°; yield 3·883 g., 7·92%), which was identified by the mixed melting-point method.

4-*Anilino*-2-*phenyl*-3 : 6 (or 1 : 6)-*dimethylpyrimidinium iodide* (VIII, *a* or *b*) crystallises from moist alcohol in long, colourless needles containing $2H_2O$, which is lost at 110°, the dried salt then melting at 220° (corr.). It is sparingly soluble in water and organic solvents (Found, in air-dried salt: H_2O, 8·8, 8·4; I, 29·0. $C_{18}H_{17}N_3,HI,2H_2O$ requires H_2O, 8·2; I, 28·9%. Found, in dried salt: C, 53·7, 53·8; H, 4·5, 4·7. $C_{18}H_{17}N_3,HI$ requires C, 53·6; H, 4·5%).

The *chloride* was prepared by digesting the above salt in hot water with silver chloride. It crystallises from water in fine, colourless needles containing $1H_2O$, which is lost at 110°, the dried salt then melting at 231—232° (corr.). It is fairly readily soluble in water or alcohol (Found, in air-dried salt: H_2O, 4·7. $C_{18}H_{17}N_3,HCl,H_2O$ requires H_2O, 5·5%. Found, in dried salt: C, 69·5, 69·3; H, 5·8, 5·8. $C_{18}H_{17}N_3,HCl$ requires C, 69·3; H, 5·8%).

4-*Phenylimino*-2-*phenyl*-3 : 6 (or 1 : 6)-*dimethyl*-3 : 4 (or 1 : 4)-*dihydropyrimidine* (IX, *a* or *b*) was prepared by basifying the aqueous solution of the above chloride with sodium carbonate, collecting the precipitated yellow base with chloroform and removing the solvent,